Supplementary Information

Facile Access to a Heterocyclic, sp^3-Rich Chemical Scaffold *via* a Tandem Condensation/Intramolecular Nitrone-Alkene [3+2] Cycloaddition Strategy

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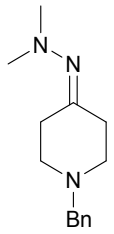
1. General details

Reagents were purchased directly from commercial suppliers. Solvents, unless otherwise stated, were purchased in reagent grade or anhydrous quality and used as received. THF was distilled from Na/benzophenone under $Ar_{(g)}$ immediately prior to use. All reactions were performed under an air atmosphere unless otherwise stated.

Nuclear Magnetic Resonance (NMR) spectra were recorded on a 400 MHz (Bruker® DPX400, or AV400) NMR spectrometer in $CDCl_3$ or CD_3OD at 300 K. All spectra were referenced to the residual hydrogen solvent peaks $CHCl_3$ or CHD_2OD: for ^1H NMR ($CHCl_3$ δ = 7.26 ppm, CHD_2OD δ = 3.33) and the solvent peak for $^{13}C\{^1H\}$ NMR ($CDCl_3$ δ = 77.16 ppm, CD_3OD δ = 49.0). NMR Chemical shifts (δ) are reported in ppm; coupling constants (*J*) are reported in Hz; splitting patterns are assigned s = singlet, d = doublet, t = triplet, q = quartet, br = broad signal and app. = the apparent multiplicity. High-resolution mass spectrometry (HRMS) data was obtained using a Bruker® MicroTOF spectrometer and measured using electrospray ionization (ESI) in the positive mode. All samples for HRMS were prepared as dilute solutions in methanol. Infrared spectra were recorded on a Bruker® Tensor27 FTIR spectrometer using a solution cell containing dilute samples dissolved in chloroform, and selected diagnostic signals are reported in cm^{-1}. Melting points were determined on a Stuart Scientific SMP3 melting point apparatus and are uncorrected. *In vacuo* refers to evaporation at reduced pressure using a rotary evaporator. Reactions were monitored by thin layer chromatography (TLC) using aluminium backed silica plates with a fluorescent dye (λ = 254 nm), and visualised under UV illumination in addition to staining with basic $KMnO_4$ or Dragendorff reagent dips.

2. Experimental procedures and analytical data

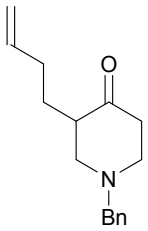
1-Benzyl-4-(2,2-dimethylhydrazono)piperidine (5a)



1-Benzyl-4-piperidinone **4a** (44.6 mL, 250 mmol, 1.0 equiv.), *N*,*N*-dimethylhydrazine (22.8 mL, 300 mmol, 1.2 equiv.) and toluene (250 mL) were added to a 500 mL round-bottom flask equipped with Dean-Stark apparatus. The reaction mixture was heated at reflux for 2 hours before being cooled to room temperature. Removal of volatiles *in vacuo* gave the title compound **5a** as a yellow oil with no need for further purification (57.8 g, 250 mmol, quant. yield).

IR ($CHCl_3$)/cm^{-1}: 1640 (C=N); ^1H NMR (400 MHz, $CDCl_3$) δ 7.34–7.23 (m, 5H), 3.53 (s, 2H), 2.65 (app. t, J = 5.9 Hz, 2H), 2.58 (app. t, J = 5.9 Hz, 2H), 2.52 (app. t, J = 6.0 Hz, 2H), 2.43 (s, 6H), 2.38 (app. t, J = 5.9 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.0, 138.4, 129.0, 128.3, 127.1, 62.6, 53.9, 52.9, 47.5, 35.1, 28.6; HRMS (EI) calculated for $C_{14}H_{22}N_3$ $[M + H]^+$ 232.1808, found 232.1813.

1-Benzyl-3-(but-3-en-1-yl)piperidin-4-one (6)

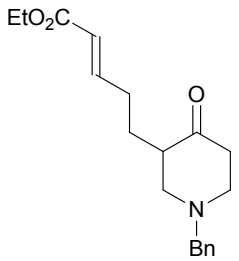


A solution of 1-benzyl-4-(2,2-dimethylhydrazono)piperidine **5 a** (27.7 g, 120 mmol, 1.0 equiv.) in anhydrous THF (300 mL) was cooled to 0 °C using an ice bath under argon. A 2.5 M solution of *n*BuLi in hexanes (52.8 mL, 132 mmol, 1.1 equiv.) was added dropwise over a period of 30 minutes before being stirred for a further 15 minutes at 0 °C. The resulting dark red solution was cooled to -78 °C using a dry ice/acetone cooling bath and neat 4-bromo-1-butene (18.2 mL, 180 mmol, 1.5 equiv.) was added dropwise over 20 minutes with vigorous stirring. The reaction mixture was stirred at -78 °C for 1 hour. A 2 M aqueous HCl solution (200 mL) was added and the reaction mixture allowed to warm to room temperature before being stirred for 2 hours. The pH was adjusted to 9–10 using 2 M NaOH solution then the phases separated. The aqueous phase was extracted using dichloromethane (3 × 100 mL), then the combined organic extracts were washed with brine (100 mL), dried ($MgSO_4$), filtered and concentrated *in vacuo* to give an orange oil (31.1 g). The residue was purified by silica gel

column chromatography (1:4 ethyl acetate:petroleum ether, R_f 0.26) to afford the title compound **6** as a colourless oil (23.6 g, 97.2 mmol, 81%).

IR ($CHCl_3$)/cm^{-1}: 1710 (C=O); ^1H NMR (400 MHz, $CDCl_3$) δ 7.37–7.24 (m, 5H), 5.73 (ddt, *J* = 16.9, 10.2, 6.6 Hz, 1H), 4.99–4.93 (m, 2H), 3.64 (d, *J* = 13.2 Hz, 1H), 3.57 (d, *J* = 13.2 Hz, 1H), 3.05–2.95 (m, 2H), 2.58–2.45 (m, 3H), 2.39–2.35 (m, 1H), 2.21 (dd, *J* = 11.1, 9.8 Hz, 1H), 2.05–1.99 (m, 2H), 1.96–1.87 (m, 1H), 1.33–1.25 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 210.8, 138.3, 138.1, 128.9, 128.4, 127.3, 115.1, 61.9, 58.6, 53.7, 49.0, 41.0, 31.2, 26.5; HRMS (EI) calculated for $C_{16}H_{22}NO$ $[M + H]^+$ 244.1696, found 244.1700.

(*E*)-Ethyl 5-(1-benzyl-4-oxopiperidin-3-yl)pent-2-enoate (3a)



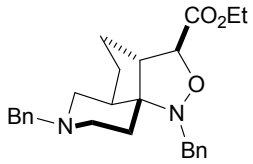
1-Benzyl-3-(but-3-en-1-yl)piperidin-4-one **6** (10.0 g, 41.2 mmol, 1.0 equiv.) was dissolved in anhydrous diethyl ether (300 mL) in a 1 L three-necked flask equipped with a reflux condenser under a nitrogen atmosphere. Ethyl acrylate (13.4 mL, 123 mmol, 3.0 equiv.) and CuI (238 mg, 1.25 mmol, 3 mol%) were added and the solution heated under reflux with stirring. A solution of Grubbs II catalyst (531 mg, 0.625 mmol, 1.5 mol%) in anhydrous diethyl ether (200 mL) was added in 20 mL portions every 10 minutes over 1.5 hours. The reaction mixture was stirred at reflux for a further 1.5 hours. After cooling to room temperature, adsorption onto silica gel and removal of diethyl ether *in vacuo*, the crude material was purified directly by silica gel column chromatography (1:2 ethyl acetate:petroleum ether, R_f 0.24) to afford the title compound **3a** (*E*:*Z* 11:1) as a brown oil (11.6 g, 36.8 mmol, 89%).

IR ($CHCl_3$)/cm^{-1}: 1715 (C=O), 1655 (C=O); ^1H NMR (400 MHz, $CDCl_3$) δ 7.35–7.27 (m, 5H), 6.89 (dt, *J* = 15.6, 6.9 Hz, 1H), 5.77 (dt, *J* = 15.6, 1.5 Hz, 1H), 4.18 (q, *J* = 7.1 Hz, 2H), 3.64 (d, *J* = 13.1 Hz, 1H), 3.57 (d, *J* = 13.1 Hz, 1H), 3.04–2.98 (m, 2H), 2.60–2.45 (m, 3H), 2.37 (dt, *J* = 6.7, 3.7 Hz, 1H), 2.24–2.11 (m, 3H), 1.96 (ddt, *J* = 13.7, 8.7, 6.9 Hz, 1H), 1.39–1.32 (m, 1H), 1.28 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 210.5, 166.7, 148.3, 138.2, 129.0, 128.6, 127.5, 122.0, 62.0, 60.3, 58.7, 53.8, 49.0, 41.1, 29.8, 25.9, 14.4; HRMS (EI) calculated for $C_{19}H_{26}NO_3$ $[M + H]^+$ 316.1907, found 316.1900.

General Procedure A: tandem condensation/nitrone-alkene [3+2] cycloaddition

3a (0.33 mmol, 1.0 equiv.), *N*-monosubstituted hydroxylamine hydrochloride (0.50 mmol, 1.5 equiv.), NaOAc (0.99 mmol, 3.0 equiv.) and toluene (11 mL) were added to a round-bottom flask equipped with a reflux condenser and Dean-Stark trap. The reaction mixture was heated under reflux with vigorous stirring. Once complete, the reaction mixture was cooled to room temperature and the solvent removed *in vacuo*. The residue was taken up in dichloromethane (5 mL) and washed with saturated aqueous $NaHCO_3$ (2 × 3 mL). The dichloromethane layer was dried over $MgSO_4$, filtered, then solvent removed *in vacuo*. The crude material was purified by silica gel column chromatography to give the corresponding isoxazolidine product.

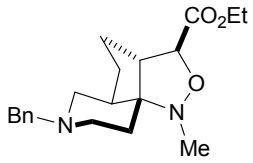
***rel*-(3*S*,3a*R*,5a*R*,9a*R*)-Ethyl-1,7-dibenzyldecahydroisoxazolo[3',4':2,3]cyclopenta[1,2-c] pyridine-3-carboxylate (2a)**



A mixture of **3a** (4.50 g, 14.3 mmol, 1.0 equiv.), *N*-benzylhydroxylamine hydrochloride (3.43 g, 21.4 mmol, 1.5 equiv.), NaOAc (5.91 g, 42.8 mmol, 3.0 equiv.) and toluene (450 mL) was heated under reflux for 18 hours according to General Procedure **A** with purification by silica gel chromatography (3:4 ethyl acetate:petroleum ether, R_f 0.32) affording the title compound **2a** as a pale yellow oil (3.99 g, 9.50 mmol, 66%).

IR ($CHCl_3$)/cm^{-1}: 1744 (C=O); ^1H NMR (400 MHz, $CDCl_3$) δ 7.43–7.24 (m, 10H), 4.27–4.13 (m, 3H), 4.04 (d, *J* = 14.8 Hz, 1H), 3.97 (d, *J* = 14.8 Hz, 1H), 3.51 (app. s, 2H), 2.94–2.87 (m, 1H), 2.83–2.77 (m, 2H), 2.32–2.10 (m, 3H), 2.10–1.91(m, 4H), 1.79–1.72 (m, 1H), 1.50–1.44 (m, 1H), 1.27 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.7, 139.1, 138.5, 129.1, 128.3, 128.2, 127.1, 126.9, 83.7, 76.0, 63.1, 61.1, 55.9, 54.8, 54.6, 51.1, 40.6, 30.4, 29.0, 26.6, 14.3; HRMS (EI) calculated for $C_{26}H_{33}N_2O_3$ $[M + H]^+$ 421.2486, found 421.2495.

***rel*-(3*S*,3a*R*,5a*R*,9a*R*)-Ethyl-7-benzyl-1-methyldecahydroisoxazolo[3',4':2,3]cyclopenta[1,2-c]pyridine-3-carboxylate (2b)**



A mixture of **3a** (500 mg, 1.59 mmol, 1.0 equiv.), *N*-methylhydroxylamine hydrochloride (200 mg, 2.38 mmol, 1.5 equiv.), NaOAc (658 mg, 4.77 mmol, 3.0 equiv.) and toluene (53 mL) was heated at reflux for 18 hours according to General Procedure **A** with purification by silica gel chromatography (ethyl acetate, R_f 0.30) affording the title compound **2b** as a colourless oil (336 mg, 0.98 mmol, 61%).

IR ($CHCl_3$)/cm^{-1}: 1742 (C=O); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31–7.30 (m, 4H), 7.27–7.22 (m, 1H), 4.21 (dtt, *J* = 10.8, 7.2, 3.7 Hz, 2H), 4.15 (d, *J* = 5.0 Hz, 1H), 3.46 (app. s, 2H), 2.83 (ddd, *J* = 7.5, 4.7, 2.4 Hz, 1H), 2.68 (s, 3H), 2.67–2.61 (m, 2H), 2.22–1.97 (m, 5H), 1.90–1.76 (m, 2H), 1.74–1.69 (m, 1H), 1.51 (app. td, *J* = 8.6, 3.0, 1H), 1.28 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.8, 138.6, 129.0, 128.3, 127.1, 83.7, 75.8, 63.1, 61.2, 55.5, 54.9, 50.9, 40.5, 38.5, 30.0, 28.6, 25.8, 14.3; HRMS (EI) calculated for $C_{20}H_{29}N_2O_3$ $[M + H]^+$ 345.2173, found 345.2173.

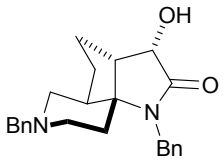
General Procedure B: Isoxazolidine (2) reduction/cyclisation

Activation of zinc: Zinc dust (3.00 g) was stirred in 1 M HCl (20 mL) for 15 minutes. The mixture was decanted and the metal washed by decantation with distilled water (4 × 25 mL). The activated zinc was transferred to a Buchner funnel lined with filter paper and rapidly washed successively with ethanol (25 mL), acetone (25 mL) and diethyl ether (2 × 25 mL) under suction. The activated zinc was quickly transferred to a round-bottom flask and dried under reduced pressure (~1 Torr) at 70 °C for 10 minutes before use.

Activated zinc dust (1.37 g, 21.0 mmol, 15 equiv.) was added to a solution of isoxazolidine **2** (1.40 mmol, 1 equiv.) in a 1:1 mixture of AcOH/H_2O (40 mL) in a 100 mL round-bottom flask equipped with a reflux condenser. The reaction mixture was stirred at 70 °C for 1.5 hours then solvents were removed *in vacuo*. The residue was dissolved in dichloromethane (20 mL) and water (20 mL) and the phases separated. The dichloromethane phase was washed with saturated aqueous $NaHCO_3$ (3 × 10 mL) and brine (1 × 10 mL), then dried ($MgSO_4$) and solvent removed *in vacuo* to give the corresponding 3-hydroxypyrrolidinones **11** as off-white foams. No further purification was necessary.

(Note: this work-up can cause an emulsion that is often very difficult to separate, particularly on large scale. We have since been using an alternative work-up for similar reactions, which eliminates emulsion formation: upon reaction completion, evaporate to dryness in vacuo, then dissolve the residue in concentrated ammonium hydroxide solution and extract with chloroform (3 ×). Wash combined extracts with brine (1 ×), dry over $MgSO_4$, filter and remove solvent in vacuo to afford the product without any need for purification.)

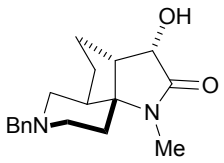
***rel*-(3*S*,3a*R*,5a*R*,9a*R*)-1,7-Dibenzyl-3-hydroxyoctahydro-1H-pyrrolo[2',3':2,3]cyclopenta[1,2-c]pyridin-2(3H)-one (11a)**



A mixture of *N*-benzylisoxazolidine **2a** (2.97 g, 7.07 mmol, 1 equiv.) and activated zinc dust (6.89 g, 106 mmol, 15 equiv.) in 1:1 AcOH/H_2O (200 mL) was treated at 70 °C for 1.5 hours according to General Procedure **B** to afford the title compound **11a** as an off-white foam (2.47 g, 6.57 mmol, 93%). The crude material was used in the following step without further purification. A small amount of **11a** was crystallised by vapour diffusion at 20 °C ($CHCl_3$/petroleum ether) for X-ray crystallographic analysis.

m.p. 173–175 °C; IR ($CHCl_3$)/cm^{-1}: 3325 (O–H), 1687 (C=O); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38–7.21 (m, 10H), 4.53 (d, *J* = 15.3 Hz, 1H), 4.53 (d, *J* = 7.8 Hz, 1H), 4.33 (d, *J* = 15.3 Hz, 1H), 3.50 (d, *J* = 13.2 Hz, 1H), 3.46 (d, *J* = 13.2 Hz, 1H), 2.93–2.87 (m, 1H), 2.87–2.83 (m, 1H), 2.70 (ddd, *J* = 11.7, 5.9, 2.0 Hz, 1H), 2.30 (app. dt, *J* = 11.7, 6.0 Hz, 1H), 2.14–2.02 (m, 2H), 1.97 (ddd, *J* = 12.7, 12.7, 4.5, 1H), 1.78–1.66 (m, 1H), 1.76 (app. t, *J* = 11.7 Hz, 1H), 1.49 (app. dt, *J* = 12.7 Hz, 2.3 Hz, 1H), 1.31–1.26 (m, 1H), 1.08–1.03 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.5, 138.3, 138.2, 129.1, 128.6, 128.4, 128.2, 127.5, 127.3, 72.3, 70.3, 62.9, 55.4, 51.0, 43.4, 42.9, 42.6, 29.8, 27.2, 20.7; HRMS (EI) calculated for $C_{24}H_{29}N_2O_2$ $[M + H]^+$ 377.2224, found 377.2228.

rel-(3*S*,3a*R*,5a*R*,9a*R*)-7-Benzyl-3-hydroxy-1-methyloctahydro-1H-pyrrolo[2',3':2,3]cyclopenta [1,2-c]pyridin-2(3H)-one (11b)



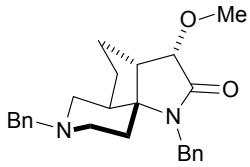
N-methylisoxazolidine **2b** (480 mg, 1.40 mmol, 1 equiv.) and activated zinc dust (1.36 g, 21.0 mmol, 15 equiv.) in 1:1 AcOH/H_2O (40 mL) was treated at 70 °C for 1.5 hours according to General Procedure **B** to afford the title compound **11b** as a sticky off-white foam (370 mg, 1.23 mmol, 88%). The crude material was used in the following step without further purification. A small amount of **11b** was crystallised by vapour diffusion at 20 °C ($CHCl_3$/petroleum ether) for X-ray crystallographic analysis.

m.p. 189–191 °C; IR ($CHCl_3$)/cm^{-1}: 3350 (O–H), 1685 (C=O); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35–7.26 (m, 5H), 4.42 (d, *J* = 7.8 Hz, 1H), 3.53 (d, *J* = 13.1 Hz, 1H), 3.48 (d, *J* = 13.1 Hz, 1H), 2.93–2.89 (m, 1H), 2.87 (ddd, *J* = 11.5, 7.9, 4.1 Hz, 1H), 2.79 (ddd, *J* = 11.7, 5.8, 2.1 Hz, 1H), 2.74 (s, 3H), 2.34 (app. dt, *J* = 11.7, 6.0 Hz, 1H), 2.15–1.98 (m, 3H), 1.82 (app. t, *J* = 11.7 Hz, 1H), 1.76–1.68 (m, 1H), 1.57–1.47 (m, 2H), 1.30–1.25 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.4, 138.2, 129.1, 128.4, 127.3, 71.1, 70.3, 63.0, 55.0, 51.0, 42.6, 41.7, 28.5, 27.4, 24.5, 20.5; HRMS (EI) calculated for $C_{18}H_{25}N_2O_2$ $[M + H]^+$ 301.1911, found 301.1903.

General Procedure C: *O*-Alkylation of polysubstituted 3-hydroxypyrrolidinones (11)

11 (1.09 mmol, 1.00 equiv.) was dissolved in anhydrous THF (8 mL) in a 25 mL round-bottom flask and cooled to 0 °C under an argon atmosphere. Sodium hydride (60% dispersion in mineral oil, 1.14 mmol, 1.05 equiv.) was added portionwise and the mixture stirred for 30 mins at 0 °C. A solution of iodomethane (1.09 mmol, 1.00 equiv.) in THF (4 mL) was added dropwise over 10 mins. The reaction mixture was stirred at 0 °C for 30 mins, then allowed to slowly warm to room temperature. After two hours at room temperature the reaction was deemed complete by mass spectrometric analysis. A few drops of water were added to quench the reaction before removal of THF *in vacuo*. The residue was taken up in a mixture of dichloromethane (25 mL) and saturated aqueous brine solution (50 mL) before the phases were separated. The aqueous phase was extracted with dichloromethane (3 × 15 mL) and the combined extracts were dried ($MgSO_4$), filtered and concentrated *in vacuo*. The crude material was purified by silica gel column chromatography to give the *O*-methylated products **12**.

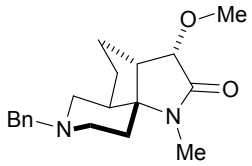
***rel*-(3*S*,3a*R*,5a*R*,9a*R*)-1,7-Dibenzyl-3-methoxyoctahydro-1H-pyrrolo[2',3':2,3]cyclopenta[1,2-c]pyridin-2(3H)-one (12a)**



11a (410 mg, 1.09 mmol, 1.00 equiv.), NaH (60% dispersion, 46 mg, 1.14 mmol, 1.05 equiv.), iodomethane (68 µL, 1.09 mmol, 1.00 equiv.) and THF (12 mL) were subjected to General Procedure **C**. Purification by silica gel column chromatography (ethyl acetate, R_f 0.45) gave the title compound **12a** as a colourless oil (278 mg, 0.711 mmol, 65%).

IR ($CHCl_3$)/cm^{-1}: 1691 (C=O); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39–7.22 (m, 10H), 4.60 (d, *J* = 15.2 Hz, 1H), 4.23 (d, *J* = 15.2 Hz, 1H), 4.13 (d, *J* = 7.5 Hz, 1H), 3.52 (s, 3H), 3.50 (d, *J* = 13.2 Hz, 1H), 3.45 (d, *J* = 13.2 Hz, 1H), 2.90–2.83 (m, 2H), 2.68 (ddd, *J* = 11.7, 5.9, 2.1 Hz, 1H), 2.26 (dt, *J* = 11.9, 6.0 Hz, 1H), 2.08–1.95 (m, 3H), 1.77–1.64 (m, 2H), 1.47–1.43 (m, 1H), 1.31–1.22 (m, 1H), 1.04–0.98 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.9, 138.6, 138.1, 129.1, 128.5, 128.4, 128.3, 127.4, 127.3, 79.0, 72.0, 62.9, 58.3, 55.3, 51.0, 43.2, 42.8, 41.3, 29.8, 27.2, 20.6; HRMS (EI) calculated for $C_{25}H_{31}N_2O_2$ $[M + H]^+$ 391.2386, found 391.2392.

***rel*-(3*S*,3a*R*,5a*R*,9a*R*)-7-Benzyl-3-methoxy-1-methyloctahydro-1H-pyrrolo[2',3':2,3]cyclopenta [1,2-c]pyridin-2(3H)-one (12b)**



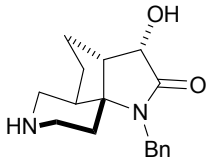
11b (400 mg, 1.33 mmol, 1.00 equiv.), NaH (60% dispersion, 56 mg, 1.40 mmol, 1.05 equiv.), iodomethane (83 µL, 1.33 mmol, 1.00 equiv.) and THF (12 mL) were subjected to General Procedure **C**. Purification by silica gel column chromatography (6:94 methanol:dichloromethane with a few drops of triethylamine, R_f 0.29) gave the title compound **12b** as a colourless oil (256 mg, 0.815 mmol, 61%).

IR ($CHCl_3$)/cm^{-1}: 1688 (C=O); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27–7.19 (m, 5H), 4.00 (d, *J* = 7.5 Hz, 1H), 3.47 (d, *J* = 13.2 Hz, 1H), 3.43 (d, *J* = 13.2 Hz, 1H), 3.40 (s, 3H), 2.88–2.77 (m, 2H), 2.72 (ddd, *J* = 11.6, 5.8, 2.1 Hz, 1H), 2.67 (s, 3H), 2.28 (dt, *J* = 11.8, 5.9 Hz, 1H), 2.07–1.92 (m, 3H), 1.76 (app. t, *J* = 11.7 Hz, 1H), 1.68 (dtd, *J* = 14.2, 10.5, 8.8 Hz, 1H), 1.53–1.44 (m, 1H), 1.43–1.40 (m, 1H), 1.21 (dd, *J* = 13.2, 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.8, 138.1, 129.0, 128.4, 127.2, 78.9, 70.5, 63.0, 58.1, 54.9, 50.9, 41.8, 40.8, 28.6, 27.3, 24.2, 20.5; HRMS (EI) calculated for $C_{19}H_{27}N_2O_2$ $[M + H]^+$ 315.2067, found 315.2054.

General Procedure D: *N*-Debenzylation by catalytic hydrogenation

A 25 mL round-bottom flask was charged with **11** or **12** (0.634 mmol, 1 equiv.), $Pd(OH)_2$ on carbon (10–20% Pd, 125 mg), ethanol (6 mL) and a magnetic stirrer bar. The air was evacuated from the reaction vessel, then the apparatus was subjected to hydrogen gas (1 atm) using a balloon. The reaction mixture was vigorously stirred (>800 rpm) at room temperature until reaction completion by mass spectrometric analysis. The heterogeneous reaction mixture was filtered through a pad of Celite®, washing with ethanol. Solvent was removed *in vacuo* and, if needed, the residue was purified by silica gel chromatography to give **13**.

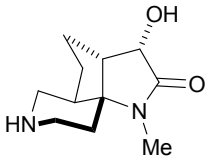
***rel*-(3*S*,3a*R*,5a*R*,9a*R*)-1-Benzyl-3-hydroxyoctahydro-1H-pyrrolo[2',3':2,3]cyclopenta[1,2-c]pyridin-2(3H)-one (13a)**



A mixture of **11a** (94 mg, 0.250 mmol, 1 equiv.), 10–20% $Pd(OH)_2/C$ (50 mg) and ethanol (2.5 mL) was stirred at room temperature for 18 hours according to General Procedure **D** to afford the title compound **13a** as a colourless oil (65 mg, 0.228 mmol, 91%).

IR ($CHCl_3$)/cm^{-1}: 3368 (broad, O–H and N–H), 1678 (C=O); ^1H NMR (400 MHz, CD_3OD) δ 7.39–7.21 (m, 5H), 4.57 (d, *J* = 7.6 Hz, 1H), 4.55 (d, *J* = 14.8 Hz, 1H), 4.31 (d, *J* = 14.8 Hz, 1H), 3.15–3.10 (m, 1H), 3.00–2.92 (m, 2H), 2.81 (app. td, *J* = 12.9, 2.8 Hz, 1H), 2.48 (app. t, *J* = 12.2 Hz, 1H), 2.31 (dt, *J* = 12.2, 5.9 Hz, 1H), 2.11–1.95 (m, 2H), 1.81–1.64 (m, 2H), 1.38–1.28 (m, 1H), 1.13–1.07 (m, 1H); ^{13}C NMR (100 MHz, CD_3OD) δ 176.9, 139.8, 129.5, 129.1, 128.5, 72.9, 71.0, 47.4, 44.5, 44.1, 43.8, 43.0, 29.3, 27.8, 21.6; HRMS (EI) calculated for $C_{17}H_{23}N_2O_2$ $[M + H]^+$ 287.1754, found 287.1748.

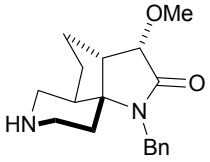
***rel*-(3*S*,3a*R*,5a*R*,9a*R*)-3-Hydroxy-1-methyloctahydro-1H-pyrrolo[2',3':2,3]cyclopenta[1,2-c]pyridin-2(3H)-one (13b)**



A mixture of **11b** (340 mg, 1.13 mmol, 1 equiv.), 10–20% $Pd(OH)_2/C$ (225 mg) and ethanol (11 mL) was stirred at room temperature for 14 hours according to General Procedure **D** to give the title compound **13b** as a colourless sticky solid (221 mg, 1.05 mmol, 93%). The compound was used in the next step without further purification.

IR ($CHCl_3$)/cm^{-1}: 3378 (broad, O–H and N–H), 1675 (C=O); ^1H NMR (400 MHz, CD_3OD) δ 4.54 (d, *J* = 7.8 Hz, 1H), 3.32–3.27 (m, 1H), 3.19 (dd, *J* = 12.6, 5.5 Hz, 1H), 3.01–2.95 (m, 2H), 2.75 (s, 3H), 2.67 (app. t, *J* = 12.6 Hz, 1H), 2.49 (dt, *J* = 12.0, 5.9 Hz, 1H), 2.17–2.09 (m, 2H), 1.85–1.73 (m, 2H), 1.64–1.54 (m, 1H), 1.41 (dd, *J* = 13.4, 8.4 Hz, 1H); ^{13}C NMR (100 MHz, CD_3OD) δ 176.0, 71.2, 70.8, 46.5, 44.1, 43.4, 41.4, 27.8, 27.3, 24.7, 21.4; HRMS (EI) calculated for $C_{11}H_{19}N_2O_2$ $[M + H]^+$ 211.1441, found 211.1431.

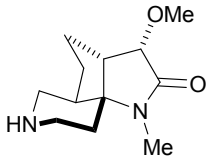
***rel*-(3*S*,3a*R*,5a*R*,9a*R*)-1-Benzyl-3-methoxyoctahydro-1H-pyrrolo[2',3':2,3]cyclopenta[1,2-c]pyridin-2(3H)-one (13c)**



A mixture of **12a** (248 mg, 0.634 mmol, 1 equiv.), 10–20% $Pd(OH)_2/C$ (175 mg) and ethanol (6 mL) was stirred at room temperature for 48 hours according to General Procedure **D**. Purification by silica gel column chromatography (1:4 methanol:dichloromethane, R_f 0.20) afforded the title compound **13c** as a sticky colourless semi-solid (167 mg, 0.558 mmol, 88%).

IR ($CHCl_3$)/cm^{-1}: 3368 (N–H), 1698 (C=O); ^1H NMR (400 MHz, CD_3OD) δ 7.47–7.45 (d, *J* = 8.3 Hz, 2H), 7.31–7.22 (m, 3H), 4.61 (d, *J* = 15.4 Hz, 1H), 4.37 (d, *J* = 7.6 Hz, 1H), 4.36 (d, *J* = 15.4 Hz, 1H), 3.48 (s, 3H), 3.42–3.38 (m, 1H), 3.26–3.13 (m, 3H), 2.79 (app. t, *J* = 12.8 Hz, 1H), 2.66–2.60 (m, 1H), 2.33 (td, *J* = 14.1, 5.3 Hz, 1H), 1.99–1.81 (m, 3H), 1.38–1.24 (m, 1H), 1.20–1.15 (m, 1H); ^{13}C NMR (100 MHz, CD_3OD) δ 175.0, 139.5, 129.5, 129.3, 128.6, 79.6, 72.3, 58.5, 45.8, 44.1, 42.9, 42.1, 41.3, 27.6, 27.2, 21.0; HRMS (EI) calculated for $C_{18}H_{25}N_2O_2$ $[M + H]^+$ 301.1911, found 301.1902.

***rel*-(3*S*,3a*R*,5a*R*,9a*R*)-3-Methoxy-1-methyloctahydro-1H-pyrrolo[2',3':2,3]cyclopenta[1,2-c]pyridin-2(3H)-one (13d)**



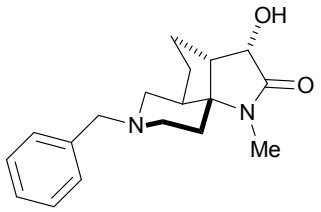
A mixture of **12b** (150 mg, 0.478 mmol, 1 equiv.), 10–20% $Pd(OH)_2/C$ (150 mg) and ethanol (4 mL) was stirred at room temperature for 24 hours according to General Procedure **D** to afford the title compound **13d** as a colourless oil (100 mg, 0.445 mmol, 93%). The compound was used in the next step without further purification.

IR ($CHCl_3$)/cm^{-1}: 3384 (N–H), 1694 (C=O); ^1H NMR (400 MHz, CD_3OD) δ 4.28 (d, J = 7.5 Hz, 1H), 3.49–3.43 (m, 1H), 3.45 (s, 3H), 3.38 (dd, J = 12.4, 5.6 Hz, 1H), 3.27–3.14 (m, 2H), 2.90 (app. t, J = 12.9 Hz, 1H), 2.77 (s, 3H), 2.71–2.65 (m, 1H), 2.31 (td, J = 14.1, 5.1 Hz, 1H), 2.03–1.89 (m, 3H), 1.69–1.59 (m, 1H), 1.52–1.47 (m, 1H); ^{13}C NMR (100 MHz, CD_3OD) δ 174.1, 79.6, 70.7, 58.4, 45.4, 42.8, 41.7, 40.3, 27.7, 25.9, 24.8, 21.0; HRMS (EI) calculated for $C_{12}H_{21}N_2O_2$ $[M + H]^+$ 225.1598, found 225.1603.

General Procedure E: Reductive amination

13 (0.134 mmol, 1.0 equiv.) was dissolved in either 1,2-dichloroethane or *N*-methylpyrrolidone (0.5 mL) in a 5 mL round-bottom flask. Aldehyde (0.201 mmol, 1.5 equiv.) and acetic acid (0.335 mmol, 2.5 equiv.) were added and the resulting mixture stirred at room temperature for 1 hour. A solution of sodium triacetoxyborohydride (0.269 mmol, 1.2 equiv.) in 1,2-dichloroethane or *N*-methylpyrrolidone (0.5 mL) was added dropwise. The reaction mixture was stirred overnight at room temperature then washed with 1 M HCl solution (2 × 5 mL). The aqueous phase was basified using saturated aqueous $NaHCO_3$ solution then extracted with ethyl acetate (3 × 5 mL), washed with water (2 × 5 mL), and the combined extracts dried ($MgSO_4$), filtered and solvent removed *in vacuo*. If necessary, the material was purified by silica gel column chromatography.

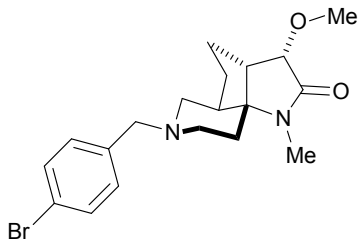
***rel*-(3*S*,3a*R*,5a*R*,9a*R*)-7-Benzyl-3-hydroxy-1-methyloctahydro-1H-pyrrolo[2',3':2,3]cyclopenta [1,2-c]pyridin-2(3H)-one (11b)**



13b (47 mg, 0.224 mmol, 1.0 equiv.), benzaldehyde (27 μL, 0.269 mmol, 1.2 equiv.), acetic acid (26 μL, 0.448 mmol, 2.0 equiv.), sodium triacetoxyborohydride (57 mg, 0.269 mmol, 1.2 equiv.) and 1,2-dichloroethane (1.25 mL) were subjected to General Procedure **E** for 18 hours at room temperature to give the title compound **11b** as a colourless foam (36 mg, 0.120 mmol, 54%).

*See data for this compound under General Procedure **B** (compound **11b**).*

(3*S*,3a*R*,5a*R*,9a*R*)-7-(4-Bromobenzyl)-3-methoxy-1-methyloctahydro-1H-pyrrolo[2',3':2,3] cyclopenta1,2-c]pyridin-2(3H)-one (1c)



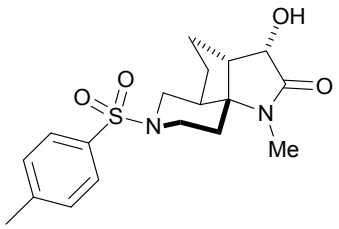
13d (30 mg, 0.134 mmol, 1 equiv.), 4-bromobenzaldehyde (37 mg, 0.201 mmol, 1.5 equiv.) and *N*-methylpyrrolidone (1 mL) were subjected to General Procedure **E** for 18 hours at room temperature. Purification by silica gel column chromatography (1:19 methanol:dichloromethane, R_f 0.35) gave the title compound **1c** as a colourless oil (27 mg, 0.069 mmol, 51%).

IR ($CHCl_3$)/cm^{-1}: 1689 (C=O); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (d, *J* = 8.4 Hz, 2H), 7.19 (d, *J* = 8.4 Hz, 2H), 4.10 (d, *J* = 7.5 Hz, 1H), 3.47 (d, *J* = 13.3 Hz, 1H), 3.46 (s, 3H), 3.42 (d, *J* = 13.3 Hz, 1H), 2.90–2.81 (m, 2H), 2.76–2.71 (m, 4H), 2.32 (dt, *J* = 11.8, 5.9 Hz, 1H), 2.11–1.96 (m, 3H), 1.83–1.67 (m, 2H), 1.60–1.44 (m, 2H), 1.29–1.23 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.9, 137.3, 131.6, 130.7, 121.1, 79.0, 70.5, 62.3, 58.2, 54.9, 50.9, 41.9, 40.9, 28.6, 27.3, 24.3, 20.5; HRMS (EI) calculated for $C_{19}H_{26}Br_1N_2O_2$ $[M(^{79}Br) + H]^+$ 393.1172, found 393.1193.

General Procedure F: *N*-Sulfonylation

13 (0.189 mmol, 1 equiv.) was dissolved in pyridine (1.2 mL) in a 5 mL round-bottom flask. The sulfonyl chloride (0.246 mmol, 1.3 equiv.) was added portionwise and the resulting mixture stirred at room temperature overnight. Removal of pyridine *in vacuo* and purification by silica gel column chromatography gave the corresponding sulfonamides.

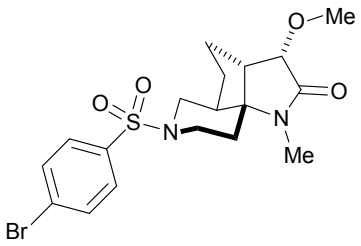
***rel*-(3*S*,3a*R*,5a*R*,9a*R*)-3-Hydroxy-1-methyl-7-tosyloctahydro-1H-pyrrolo[2',3':2,3]cyclopenta [1,2-c]pyridin-2(3H)-one (1a)**



13b (47 mg, 0.224 mmol, 1 equiv.), p-toluenesulfonyl chloride (56 mg, 0.291 mmol, 1.3 equiv.) and pyridine (1.2 mL) were subjected to General Procedure **F** for 18 hours at room temperature. Purification by silica gel column chromatography (1:9 methanol:dichloromethane, R_f 0.33) gave the title compound **1a** as a colourless solid (59 mg, 0.162 mmol, 72%).

m.p. 230 ^{o}C (decomp.); IR ($CHCl_3$)/cm^{-1}: 1691 (C=O), 1355 & 1165 (S=O); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, *J* = 8.1 Hz, 2H), 7.33 (d, *J* = 8.1 Hz, 2H), 4.35 (d, *J* = 7.8 Hz, 1H), 4.14 (bs, 1H), 3.84 (ddt, *J* = 7.3, 4.6, 2.0 Hz, 1H), 3.72 (ddd, *J* = 12.2, 6.1, 2.3 Hz, 1H), 3.66 (s, 3H), 2.65–2.59 (m, 1H), 2.43 (s, 3H), 2.41–2.32 (m, 2H), 2.14–2.02 (m, 3H), 1.62–1.50 (m, 3H), 1.35–1.27 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.5, 144.0, 133.4, 130.0, 127.6, 70.2, 69.8, 47.0, 43.8, 42.3, 41.5, 28.0, 26.8, 24.4, 21.7, 20.4; HRMS (EI) calculated for $C_{18}H_{25}N_2O_4S$ $[M + H]^+$ 365.1535, found 365.1530.

(3*S*,3a*R*,5a*R*,9a*R*)-7-((4-Bromophenyl)sulfonyl)-3-methoxy-1-methyloctahydro-1H-pyrrolo 2',3':2,3]cyclopenta[1,2-c]pyridin-2(3H)-one (1d)



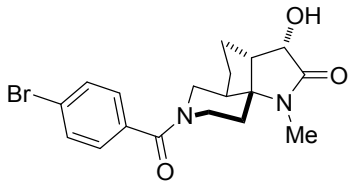
13d (24 mg, 0.107 mmol, 1 equiv.), 4-bromobenzenesulfonyl chloride (27 mg, 0.139 mmol, 1.3 equiv.) and pyridine (1.2 mL) were subjected to General Procedure **F** for 18 hours at room temperature. Purification by silica gel column chromatography (1:19 methanol:dichloromethane, R_f 0.35) gave the title compound **1d** as a colourless gum (28 mg, 0.063 mmol, 59%).

IR ($CHCl_3$)/cm^{-1}: 1698 (C=O), 1358 & 1169 (S=O); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 8.8 Hz, 2H), 7.64 (d, *J* = 8.8 Hz, 2H), 3.98 (d, *J* = 7.5 Hz, 1H), 3.85 (ddt, *J* = 7.6, 5.0, 2.2 Hz, 1H), 3.74 (ddd, *J* = 12.2, 6.1, 2.4 Hz, 1H), 3.42 (s, 3H), 2.69 (s, 3H), 2.67–2.62 (m, 1H), 2.45–2.38 (m, 2H), 2.14–2.02 (m, 3H), 1.67–1.54 (m, 3H), 1.38–1.30 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.6, 135.6, 132.8, 129.2, 128.3, 78.5, 69.7, 58.3, 47.0, 43.8, 41.7, 40.7, 28.1, 26.8, 24.3, 20.4; HRMS (EI) calculated for $C_{18}H_{23}Br_1N_2O_4S_1Na_1$ $[M(^{79}Br) + Na]^+$ 465.0454, found 465.0484.

General Procedure G: *N*-Amidation

13 (0.147 mmol, 1.5 equiv.), diisopropylethylamine (0.295 mmol, 3 equiv.) and the carboxylic acid (0.098 mmol, 1 equiv.) were stirred in DMF (0.7 mL) and the solution cooled to 0 °C before dropwise addition of a solution of HATU (0.196 mmol, 2 equiv.) in DMF (0.3 mL). The reaction mixture was stirred at room temperature for 18 hours under an inert argon atmosphere before being diluted with ethyl acetate (10 mL) and washed successively with 2 M HCl (3 × 5 mL), saturated aqueous $NaHCO_3$ solution (1 × 5 mL), brine (1 × 5 mL) then dried over $MgSO_4$. Filtration and removal of solvents *in vacuo* gave the crude material which was purified by silica gel column chromatography.

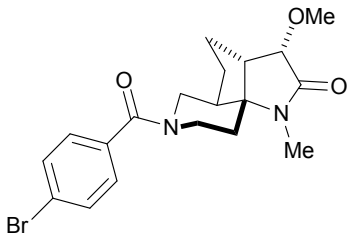
***rel*-(3*S*,3a*R*,5a*R*,9a*R*)-7-(4-Bromobenzoyl)-3-hydroxy-1-methyloctahydro-1H-pyrrolo[2',3':2,3] cyclopenta[1,2-c]pyridin-2(3H)-one (1b)**



13b (30 mg, 0.143 mmol, 2.0 equiv.), diisopropylethylamine (24 µL, 0.143 mmol, 2.0 equiv.), 4-bromobenzoic acid (14 mg, 0.071 mmol, 1.0 equiv.), HATU (54 mg, 0.143 mmol, 2.0 equiv.) and DMF (1 mL) were subjected to General Procedure **G** for 18 hours at room temperature. Purification by silica gel column chromatography (up to 1:9 methanol:dichloromethane) gave the title compound **1b** as a colourless solid (10 mg, 0.025 mmol, 36%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, *J* = 8.4 Hz, 2H), 7.30 (d, *J* = 8.4 Hz, 2H), 4.76–4.47 (m, 1H), 4.45 (br d, *J* = 7.5 Hz, 1H), 3.85–3.55 (m, 1H), 3.24–3.00 (m, 1H), 2.95 (m, 2H), 2.75 (s, 3H), 2.42–2.26 (m, 1H), 2.22–1.99 (m, 2H), 1.90–1.74 (m, 2H), 1.69–1.54 (m, 2H), 1.38–1.25 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.8, 169.7, 134.2, 131.9, 128.7, 124.4, 70.6, 69.9, 53.8, 43.0, 31.9, 29.7, 29.3, 27.1, 24.5, 14.1; HRMS (EI) calculated for $C_{18}H_{21}Br_1N_2O_3Na_1$ $[M(^{79}Br) + Na]^+$ 415.1628, found 415.0663.

(3*S*,3a*R*,5a*R*,9a*R*)-7-(4-Bromobenzoyl)-3-methoxy-1-methyloctahydro-1H-pyrrolo[2',3':2,3] cyclopenta[1,2-c]pyridin-2(3H)-one (1e)

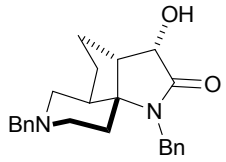


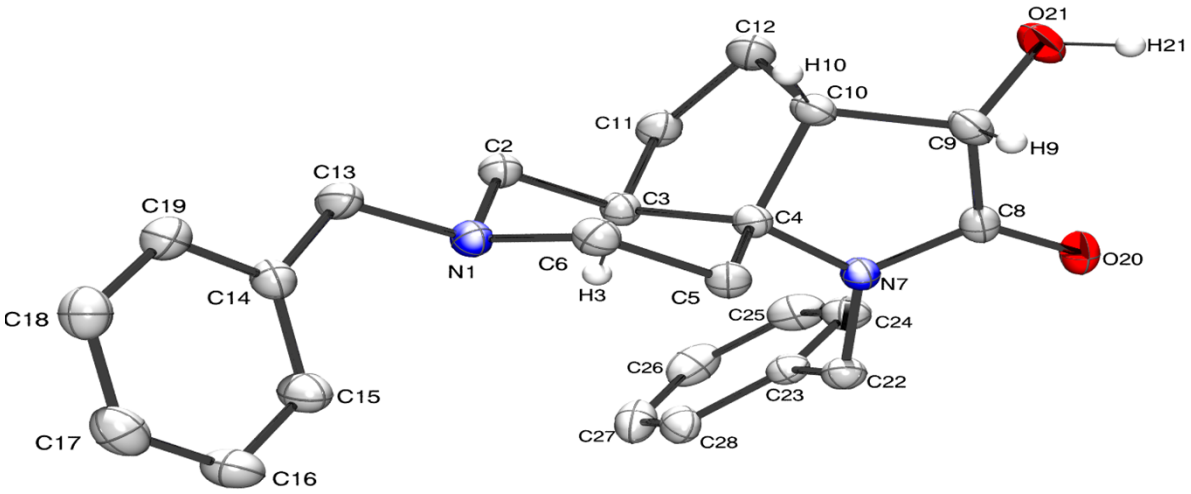
13d (33 mg, 0.147 mmol, 1.5 equiv.), diisopropylethylamine (51 µL, 0.295 mmol, 3.0 equiv.), 4-bromobenzoic acid (20 mg, 0.098 mmol, 1.0 equiv.), HATU (75 mg, 0.196 mmol, 2.0 equiv.) and DMF (1 mL) were subjected to General Procedure **G** for 18 hours at room temperature. Purification by silica gel column chromatography (1:19 methanol:dichloromethane, R_f 0.28) gave the title compound **1e** as a colourless solid (15 mg, 0.037 mmol, 38%).

IR ($CHCl_3$)/cm^{-1}: 1698 (C=O), 1630 (C=O); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, *J* = 8.5 Hz, 2H), 7.32 (d, *J* = 8.5 Hz, 2H), 4.78–4.49 (m, 1H), 4.11 (d, *J* = 7.0 Hz, 1H), 3.94–3.61 (m, 1H), 3.54 (s, 3H), 3.25–2.85 (m, 3H), 2.76 (s, 3H), 2.48–1.99 (m, 3H), 1.92–1.75 (m, 1H), 1.59–1.41 (m, 2H), 1.36–1.25 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.6, 169.8, 134.3, 132.0, 128.8, 124.6, 78.6, 70.2, 58.5, 41.5, 27.2, 24.4, 21.2 (note: not all carbon signals are visible); HRMS (EI) calculated for $C_{19}H_{23}Br_1N_2O_3Na_1$ [M(^{79}Br) + Na]$^+$ 429.0784, found 429.0790.

3. X-ray crystal structure data

Compound 11a



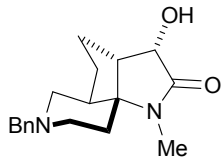


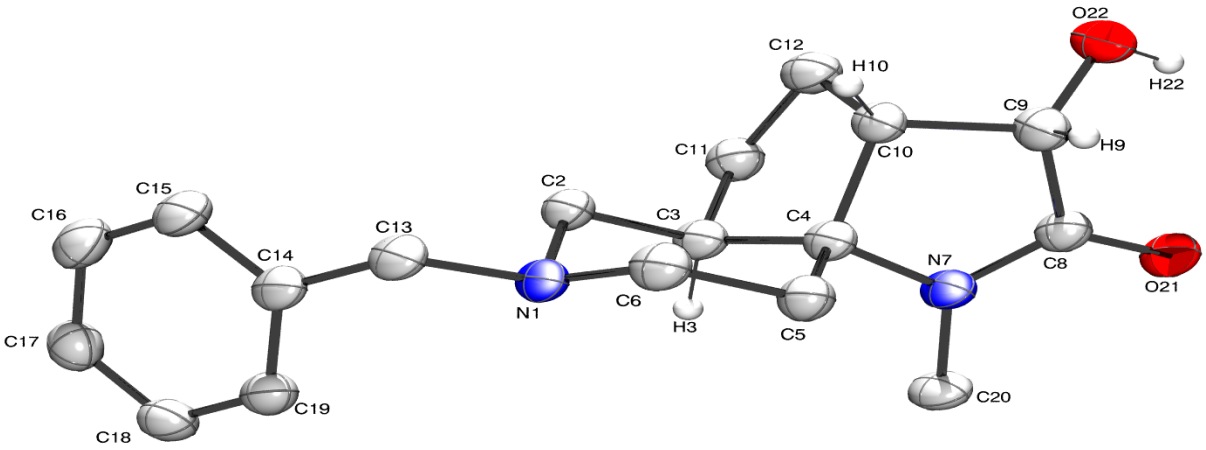
Thermal ellipsoids are shown at 50 % probability; selected hydrogens of the molecule have been omitted for clarity.

CCDC No. = **1045613**

$C_{24}H_{28}N_2O_2$ Mw = 376.48; T = 120(10) K; λ = 1.54184 Å; Monoclinic; P21/n space group; a = 11.8462(8) Å, b = 7.6966(5)Å, c = 22.1897(18) Å; α = 90°, β = 94.024(7)°, γ = 90°; V = 2018.2(3) $Å^3$; Z = 4; D = 1.239 Mg/m^3; R = 0.0423 (all data), wR = 0.0987, GoF = 1.040.

Compound 11b





Thermal ellipsoids are shown at 50 % probability; selected hydrogens of the molecule have been omitted for clarity.

CCDC No. = **1045614**

$C_{18}H_{24}N_2O_2$ Mw = 300.39; T = 120(2) K; λ = 1.54184 Å; Triclinic; P -1 space group; a = 8.0233(8) Å, b = 8.5269(8)Å, c = 12.1531(9) Å; α = 107.964(7)°, β = 98.204(8)°, γ = 97.133(7)°; V = 770.22(11) $Å^3$; Z = 2; D = 1.295 Mg/m^3; R = 0.0916 (all data), wR = 0.2499, GoF = 1.085.

4. Computational details

The computations were executed in Spartan 10. Initially the structure was minimised using molecular mechanics (MMFF). Hartree-Fock was then used (6-31G* basis set) to find the equilibrium conformer, and then again to find the equilibrium geometry.

For compound **9**:

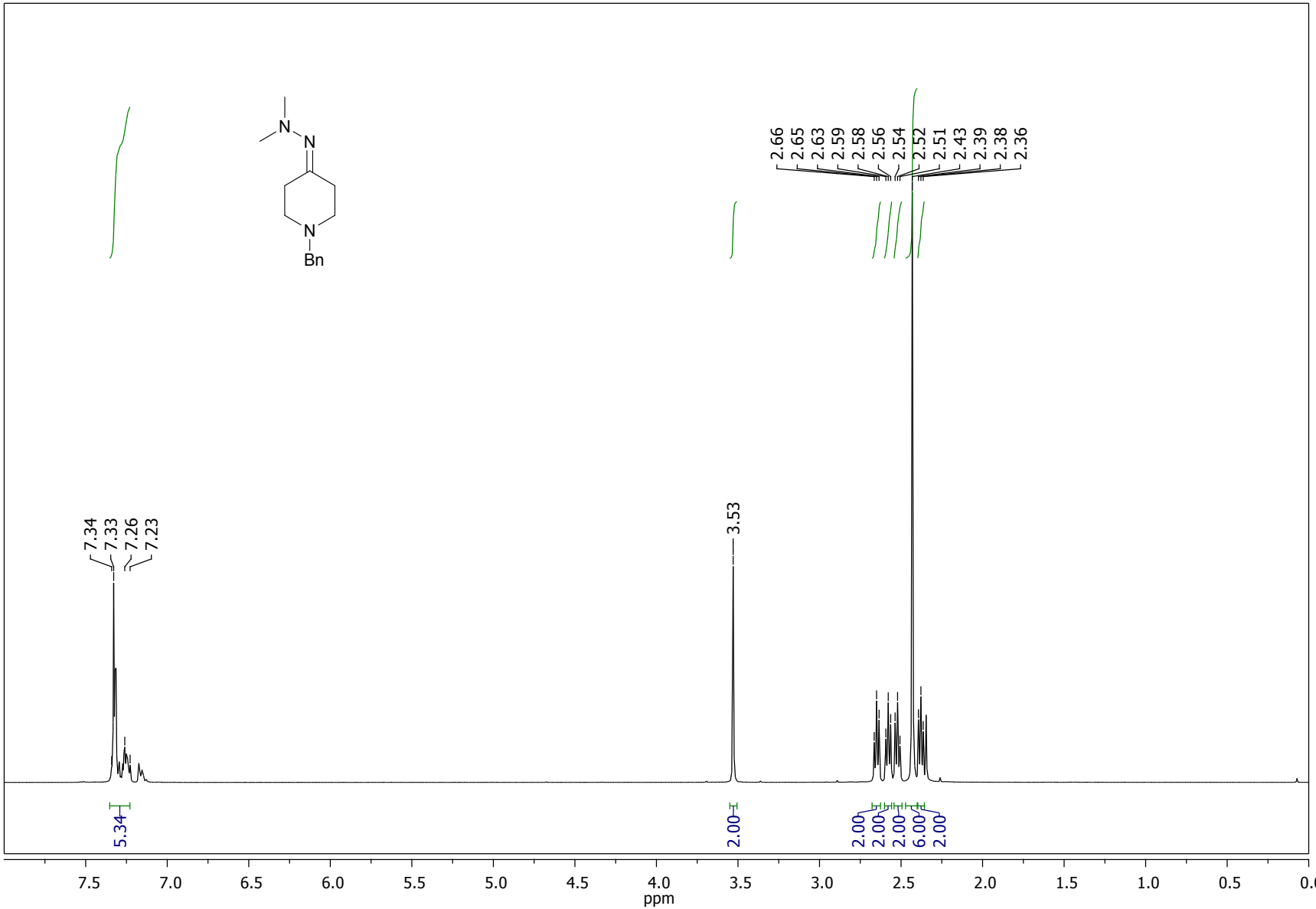
MacSPARTAN '10 Quantum Mechanics Program: (x86/Darwin) build 1.1.0v4
Job type: Frequency calculation.
Method: RHF
Basis set: 6-31G(D)
Number of shells: 156
Number of basis functions: 431
Multiplicity: 1
Parallel Job: 4 threads
SCF model: A restricted Hartree-Fock SCF calculation will be
performed using Pulay DIIS + Geometric Direct Minimization
SCF total energy: -1107.0983540 Hartrees
Reason for exit: Successful completion
Quantum Calculation CPU Time : 1:58:34.08
Quantum Calculation Wall Time: 2:06:40.80
MacSPARTAN '10 Semi-Empirical Program: (x86/Darwin) build 1.1.0
Semi-empirical Property Calculation
M0001
Guess from Archive
Energy Due to Solvation
Solvation Energy SM5.4/A -7.672
Memory Used: 10.942 Mb
Reason for exit: Successful completion
Semi-Empirical Program CPU Time : .45
Semi-Empirical Program Wall Time: .53
MacSPARTAN '10 Properties Program: (x86/Darwin) build 1.1.0
Temperature Corrections for 298.15 K
Reason for exit: Successful completion
Properties CPU Time : 4.04
Properties Wall Time: 4.16
molecule M0001 terminated normally
End- molecule "M0001" Tue Oct 21 14:31:24 2014

For compound **2b**:

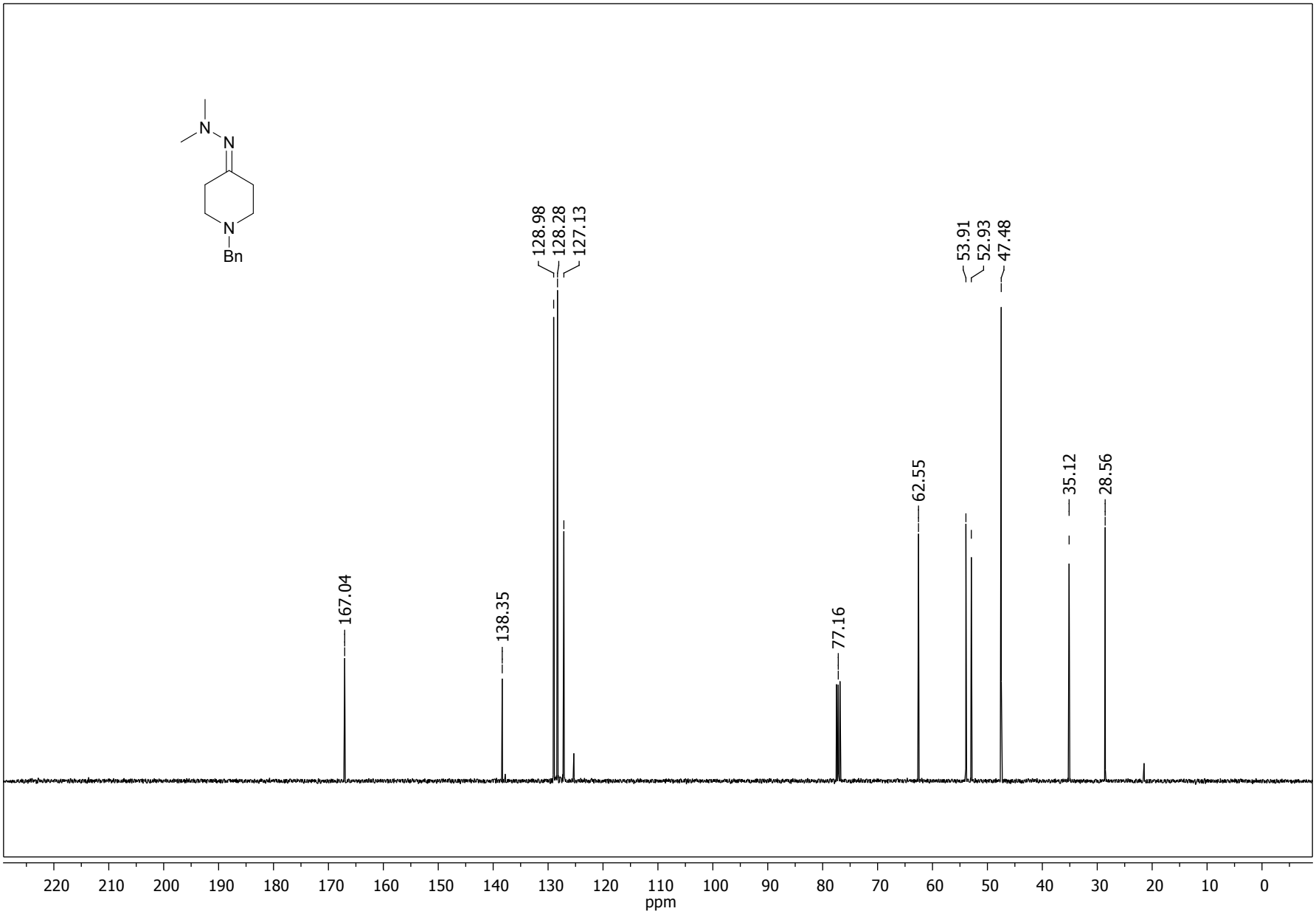
MacSPARTAN '10 Quantum Mechanics Program: (x86/Darwin) build 1.1.0v4
Job type: Frequency calculation.
Method: RHF
Basis set: 6-31G(D)
Number of shells: 156
Number of basis functions: 431
Multiplicity: 1
Parallel Job: 4 threads
SCF model:
A restricted Hartree-Fock SCF calculation will be
performed using Pulay DIIS + Geometric Direct Minimization
SCF total energy: -1107.1010451 hartrees
Reason for exit: Successful completion
Quantum Calculation CPU Time : 1:54:14.11
Quantum Calculation Wall Time: 2:01:33.31
MacSPARTAN '10 Semi-Empirical Program: (x86/Darwin) build 1.1.0
Semi-empirical Property Calculation
M0001
Guess from Archive
Energy Due to Solvation
Solvation Energy SM5.4/A -5.667
Memory Used: 10.942 Mb
Reason for exit: Successful completion
Semi-Empirical Program CPU Time : .68
Semi-Empirical Program Wall Time: .78
MacSPARTAN '10 Properties Program: (x86/Darwin) build 1.1.0
Temperature Corrections for 298.15 K
Reason for exit: Successful completion
Properties CPU Time : 5.68
Properties Wall Time: 5.83
molecule M0001 terminated normally
End- molecule "M0001" Tue Oct 21 14:26:06 2014

^{1}H and ^{13}C NMR Spectra

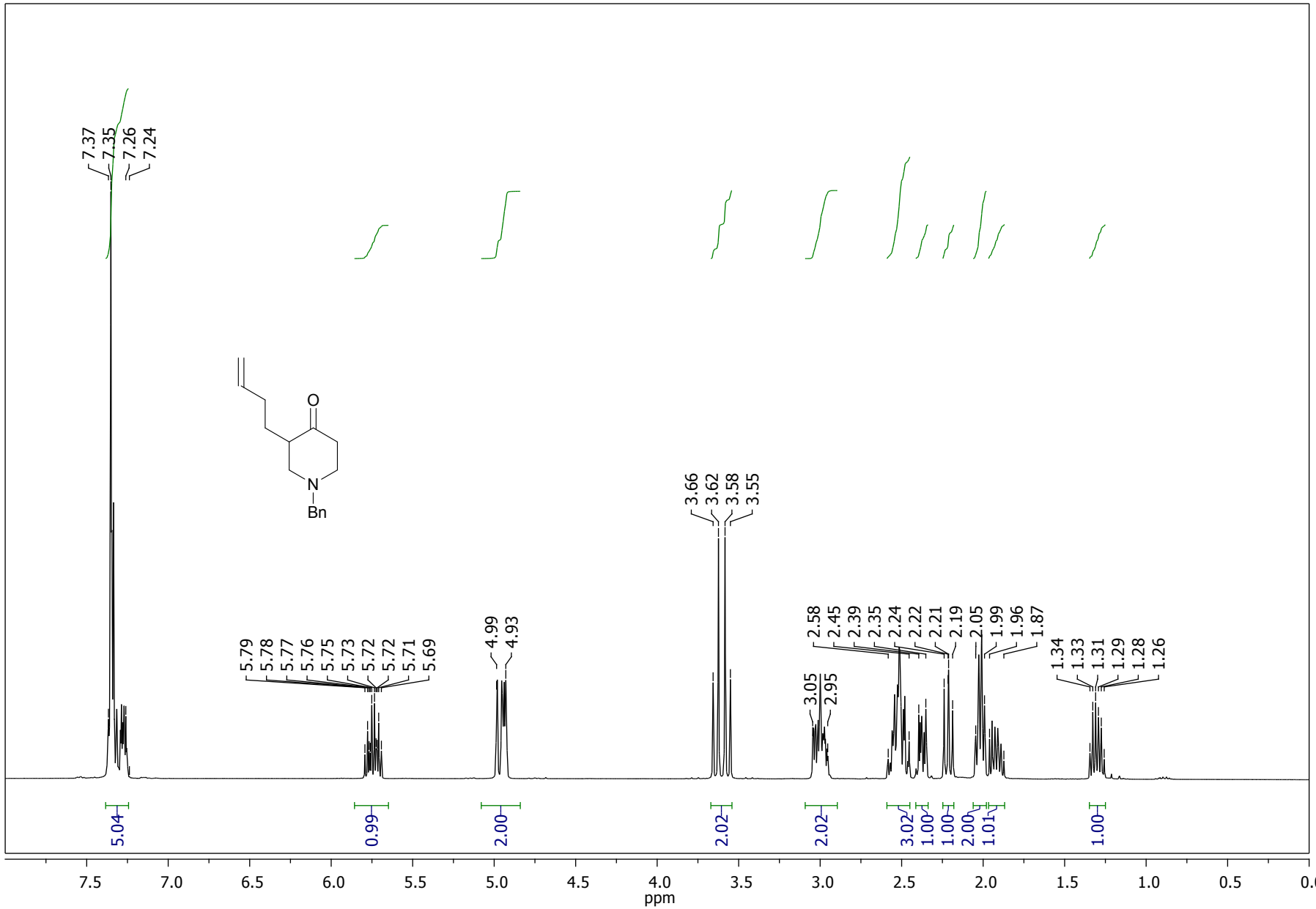
^{1}H NMR (400 MHz, $CDCl_3$) **(5a)**



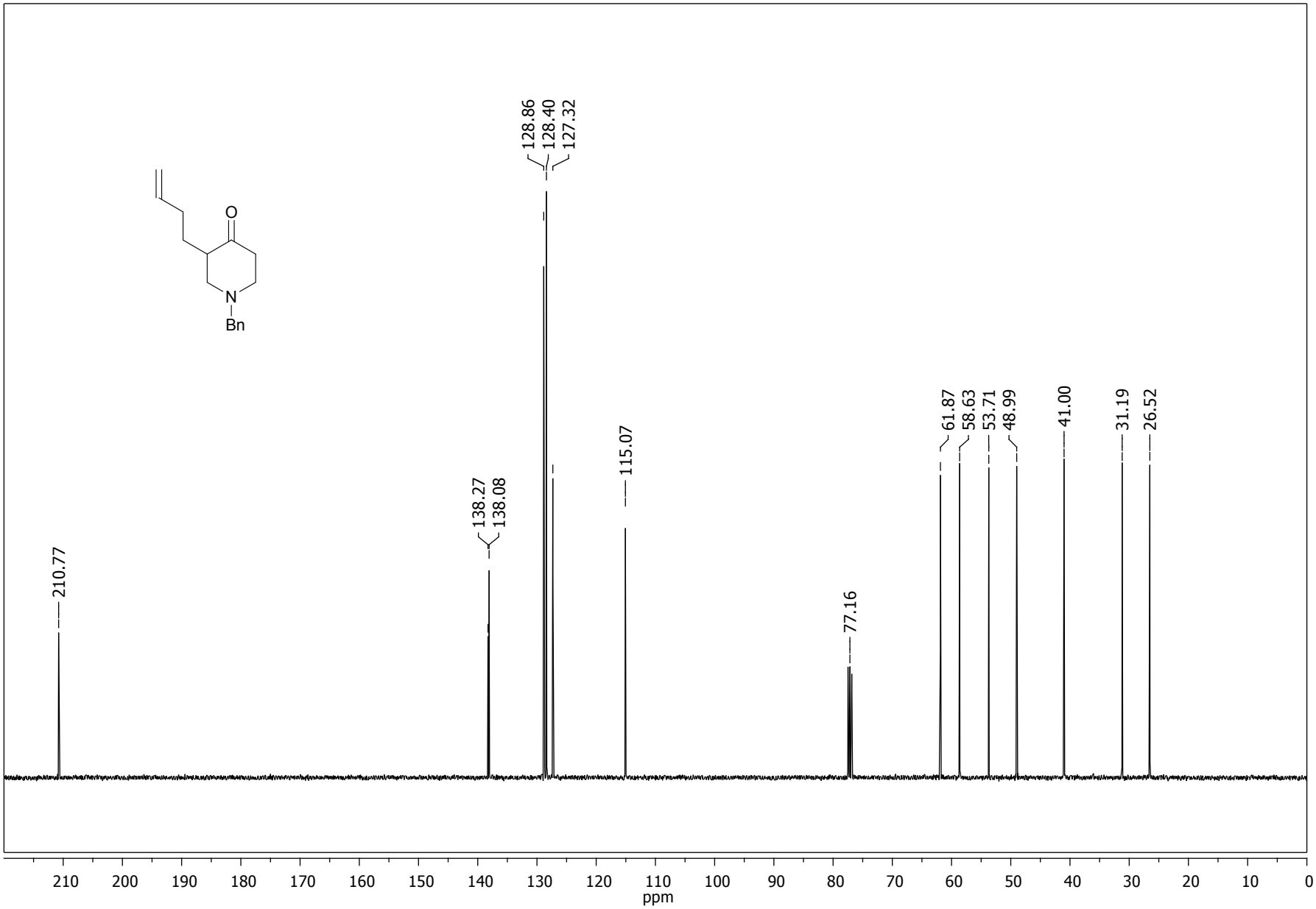
^{13}C NMR (100 MHz, $CDCl_3$) **(5a)**



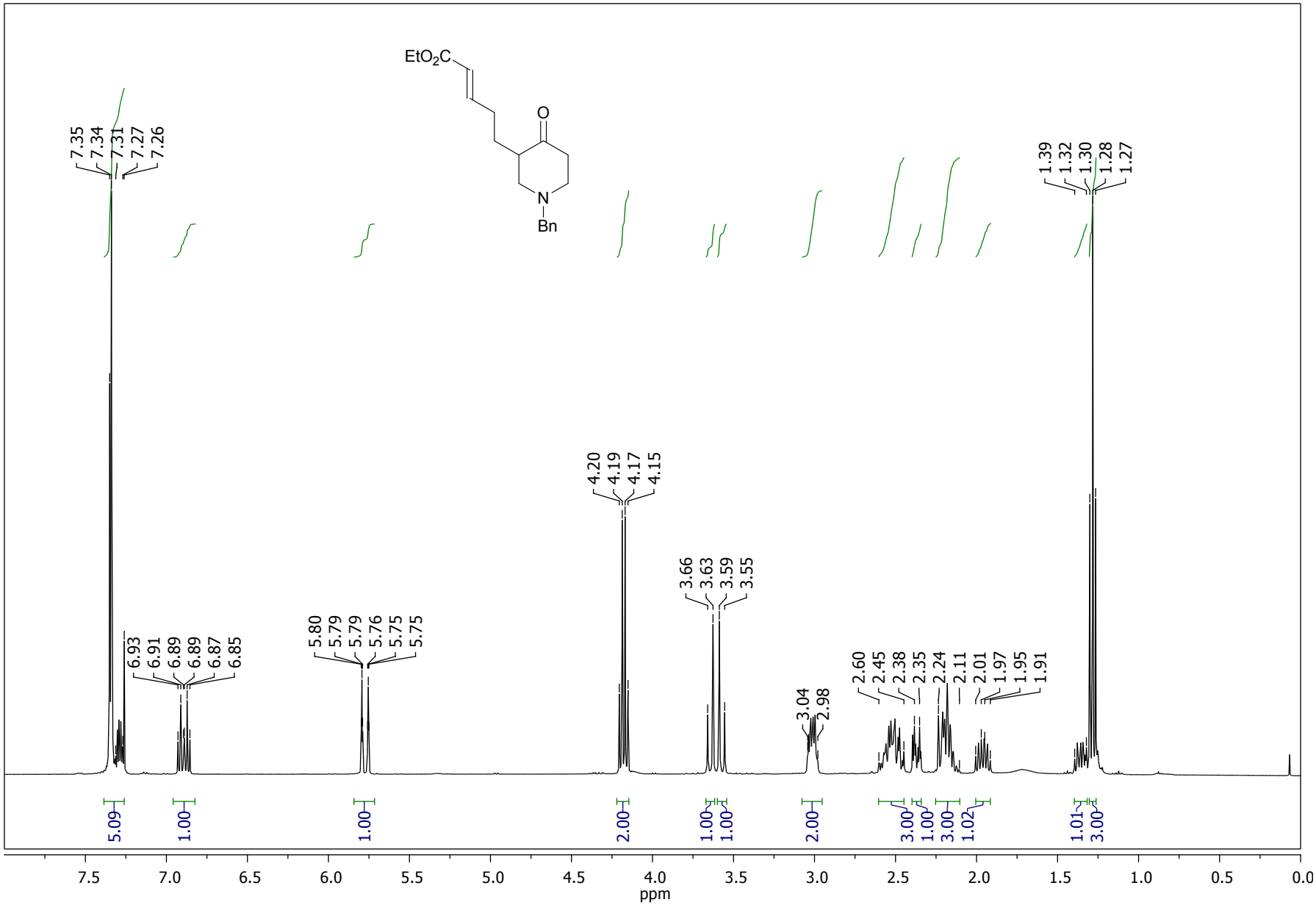
^{1}H NMR (400 MHz, $CDCl_3$) **(6)**



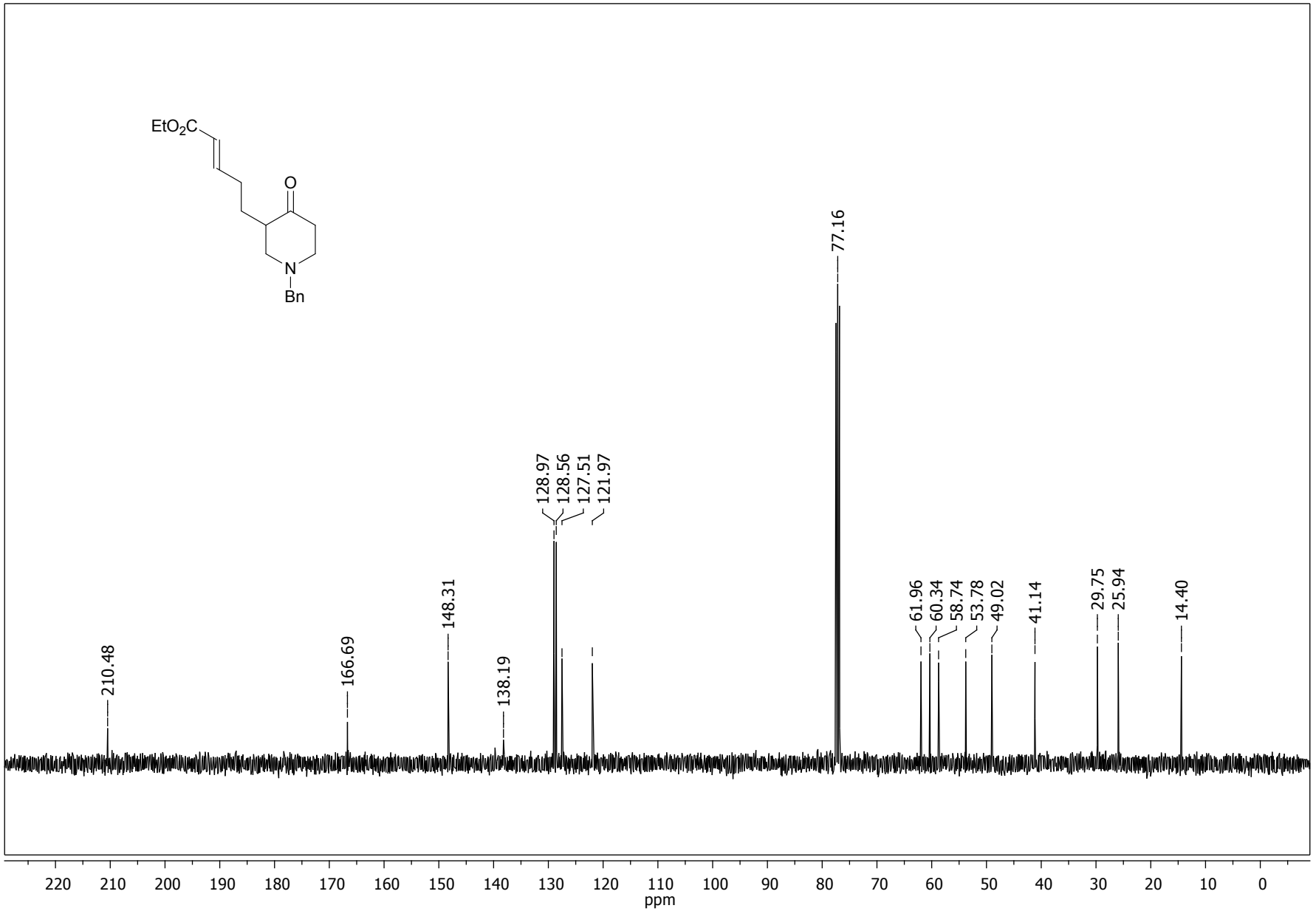
^{13}C NMR (100 MHz, $CDCl_3$) **(6)**



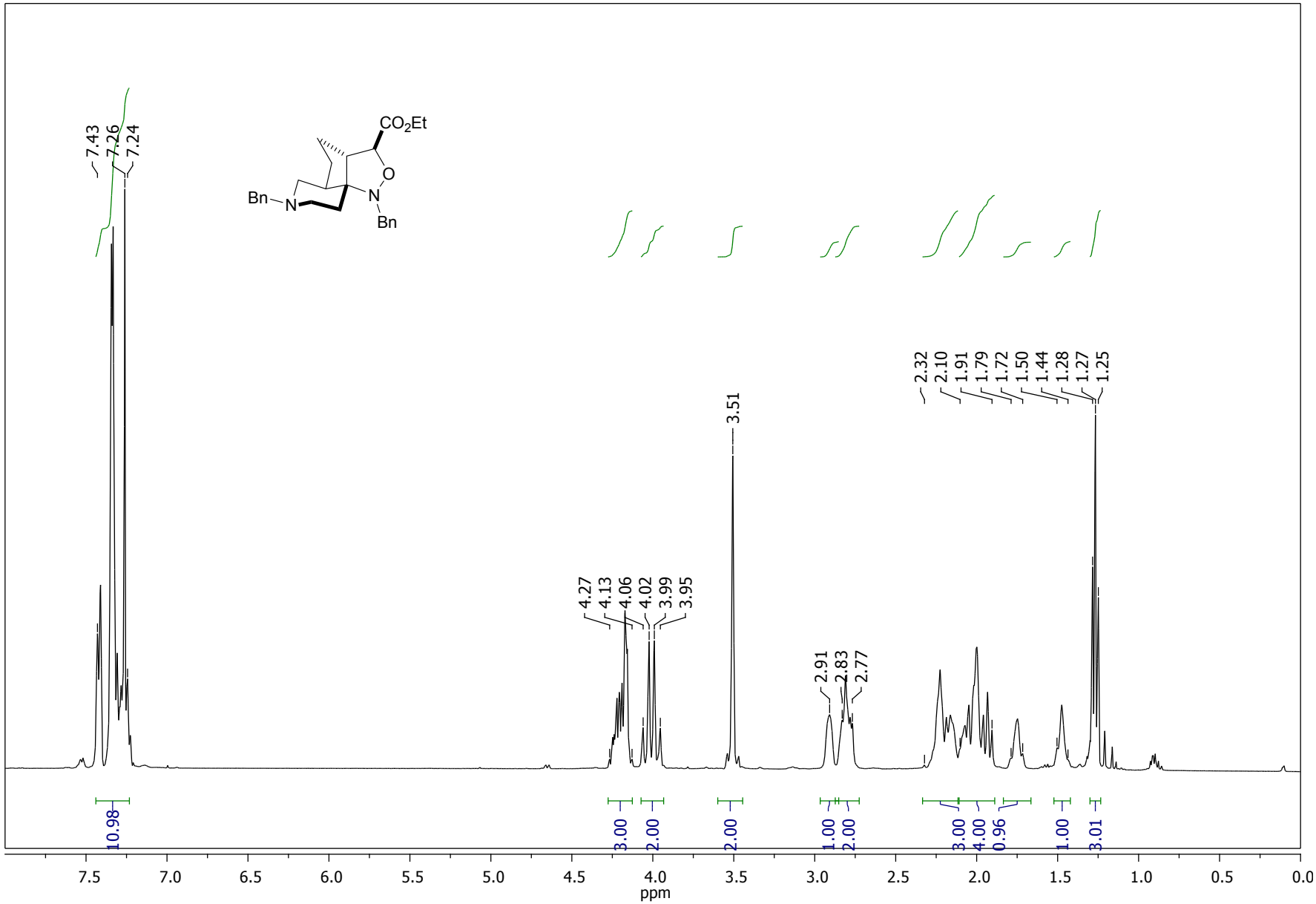
^{1}H NMR (400 MHz, $CDCl_3$) **(3a)**



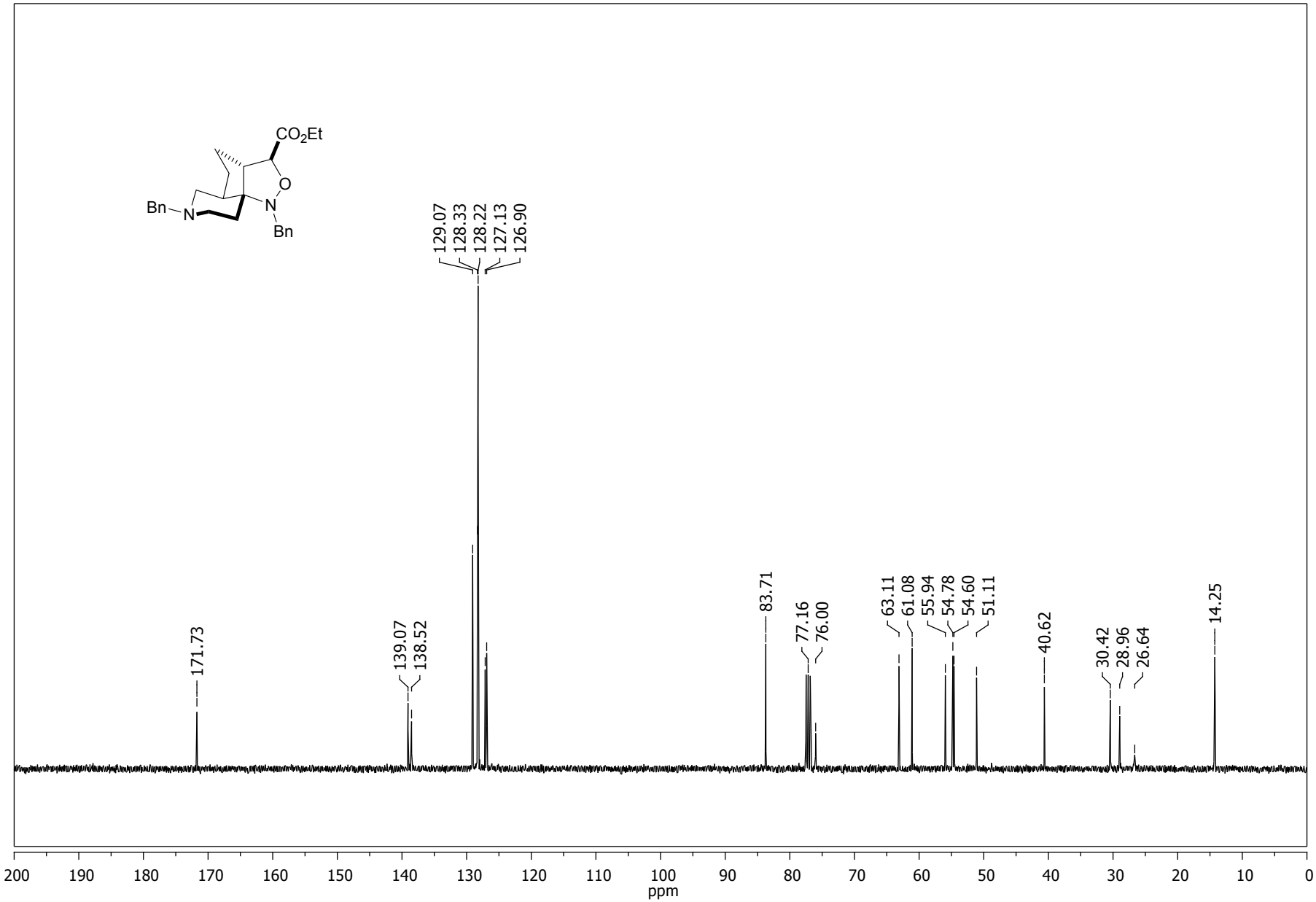
^{13}C NMR (100 MHz, $CDCl_3$) **(3a)**



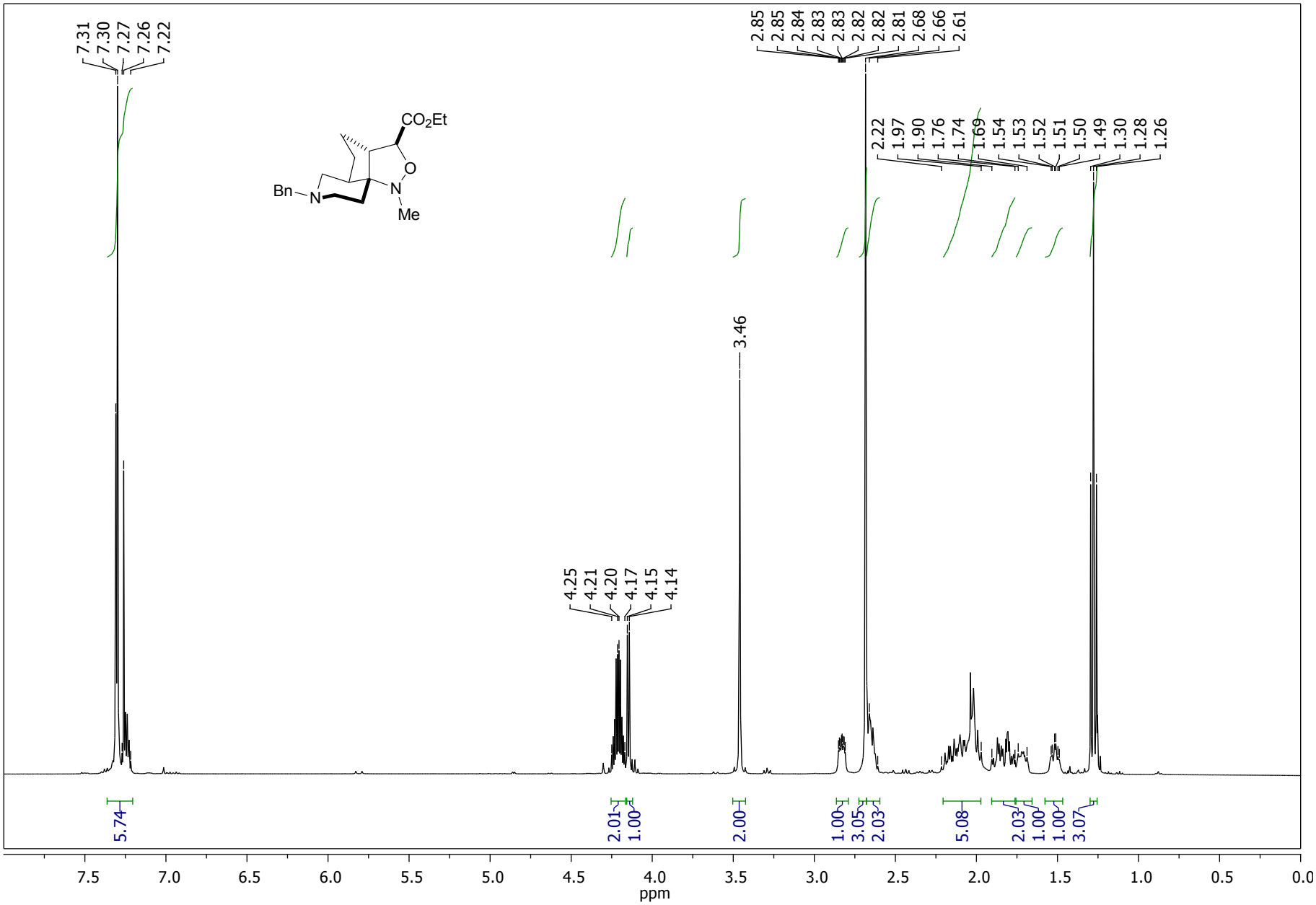
^{1}H NMR (400 MHz, $CDCl_3$) **(2a)**



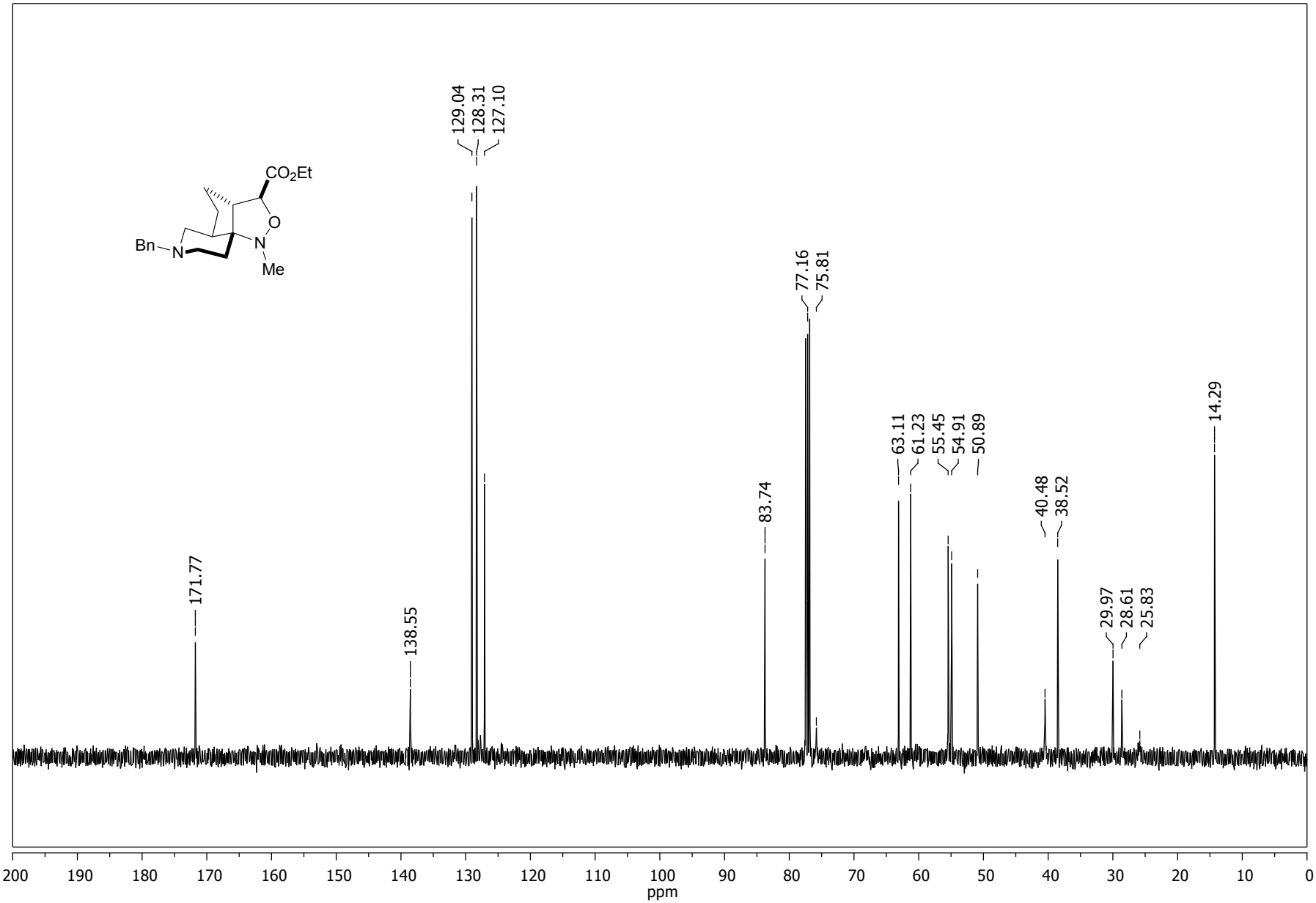
^{13}C NMR (100 MHz, $CDCl_3$) **(2a)**



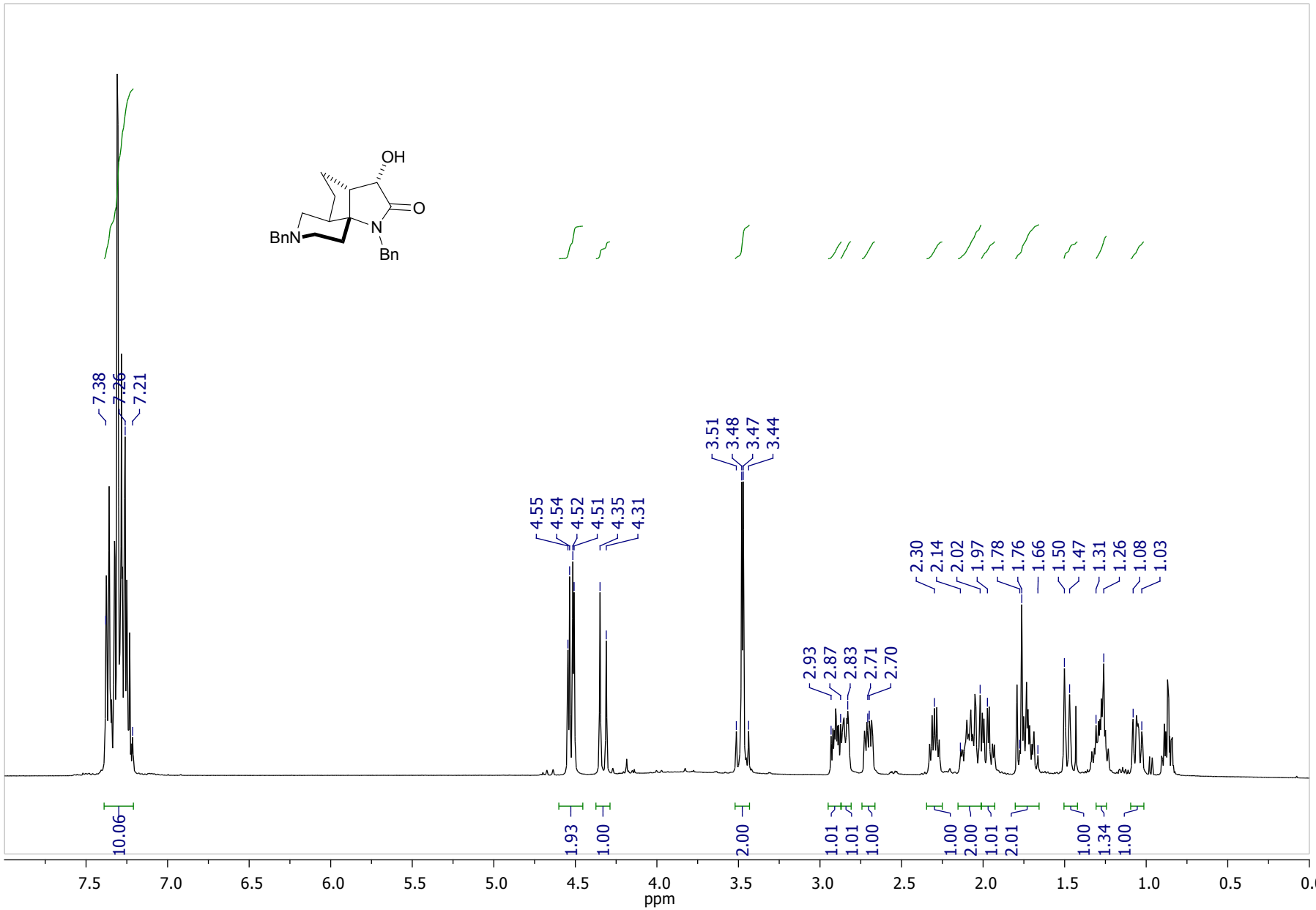
^{1}H NMR (400 MHz, $CDCl_3$) **(2b)**



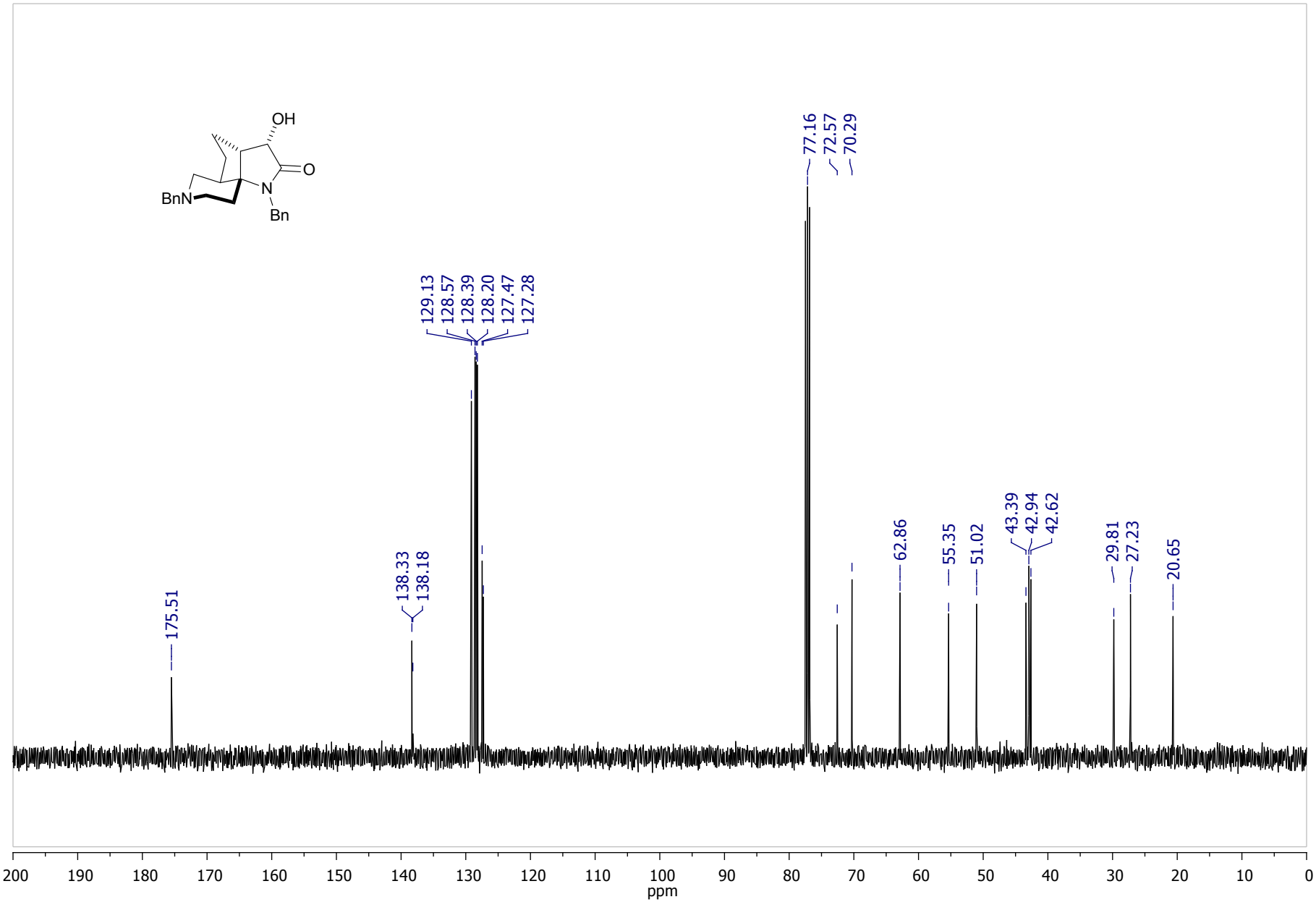
^{13}C NMR (100 MHz, $CDCl_3$) **(2b)**



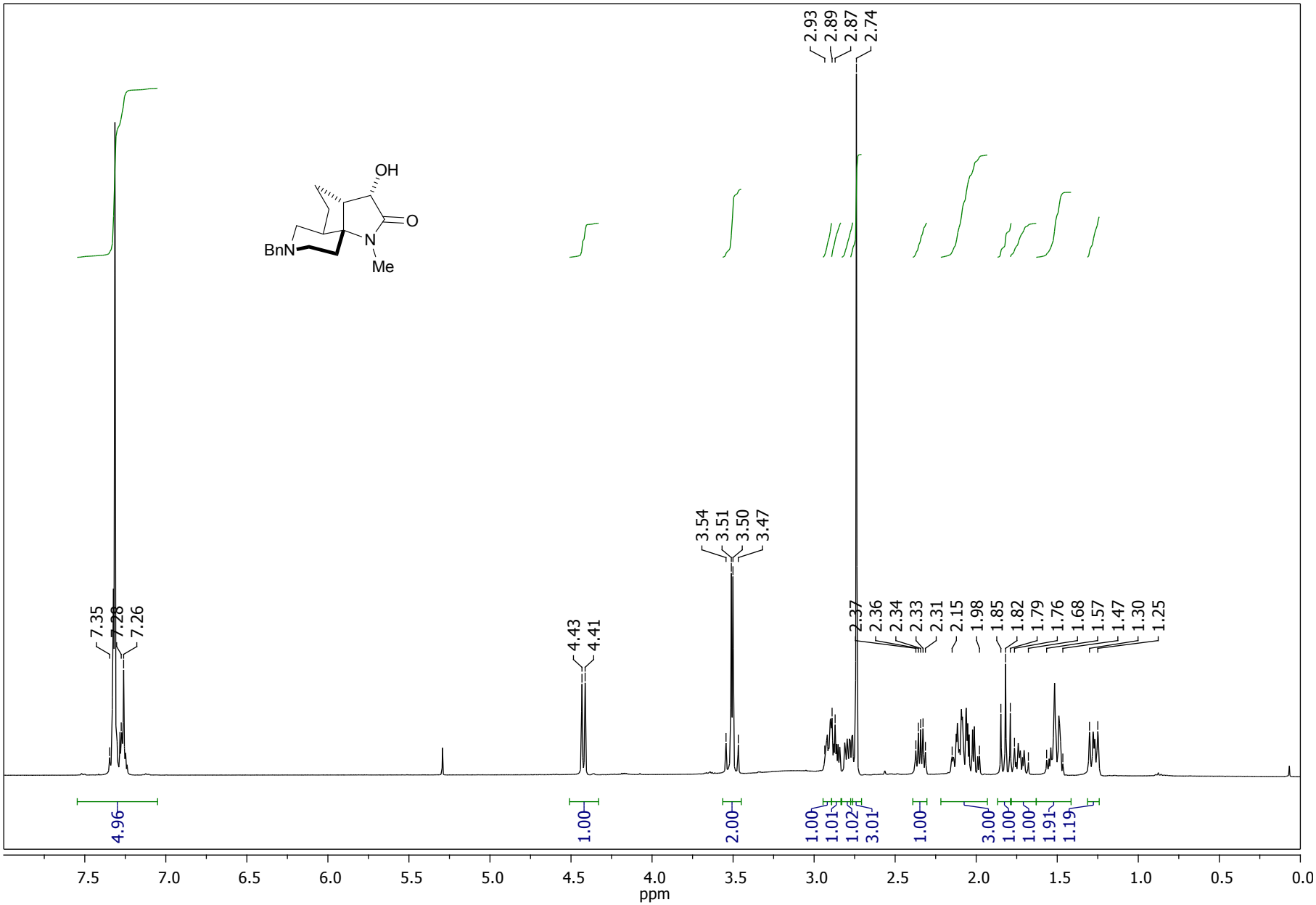
^{1}H NMR (400 MHz, $CDCl_3$) **(11a)**



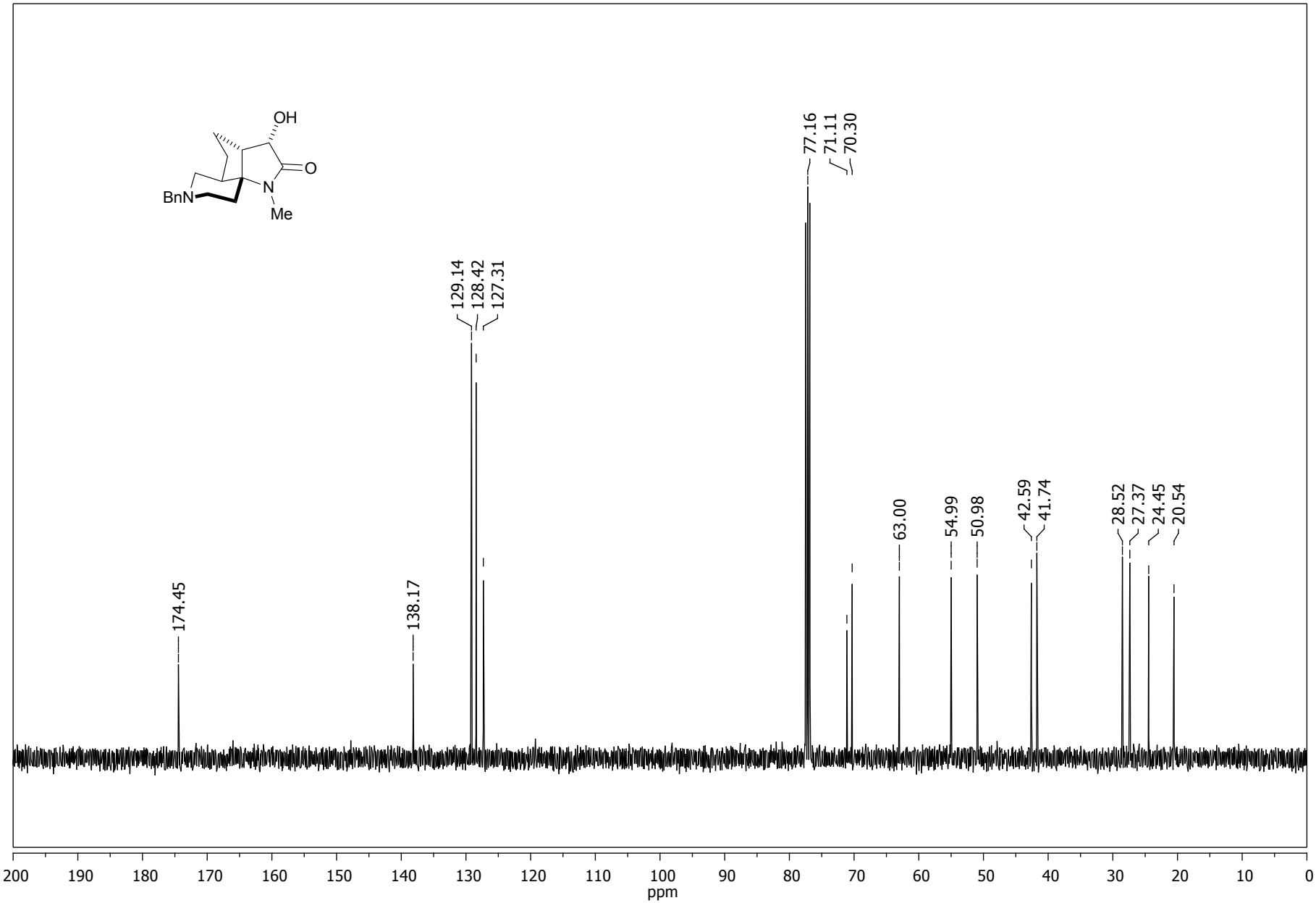
^{13}C NMR (100 MHz, $CDCl_3$) **(11a)**



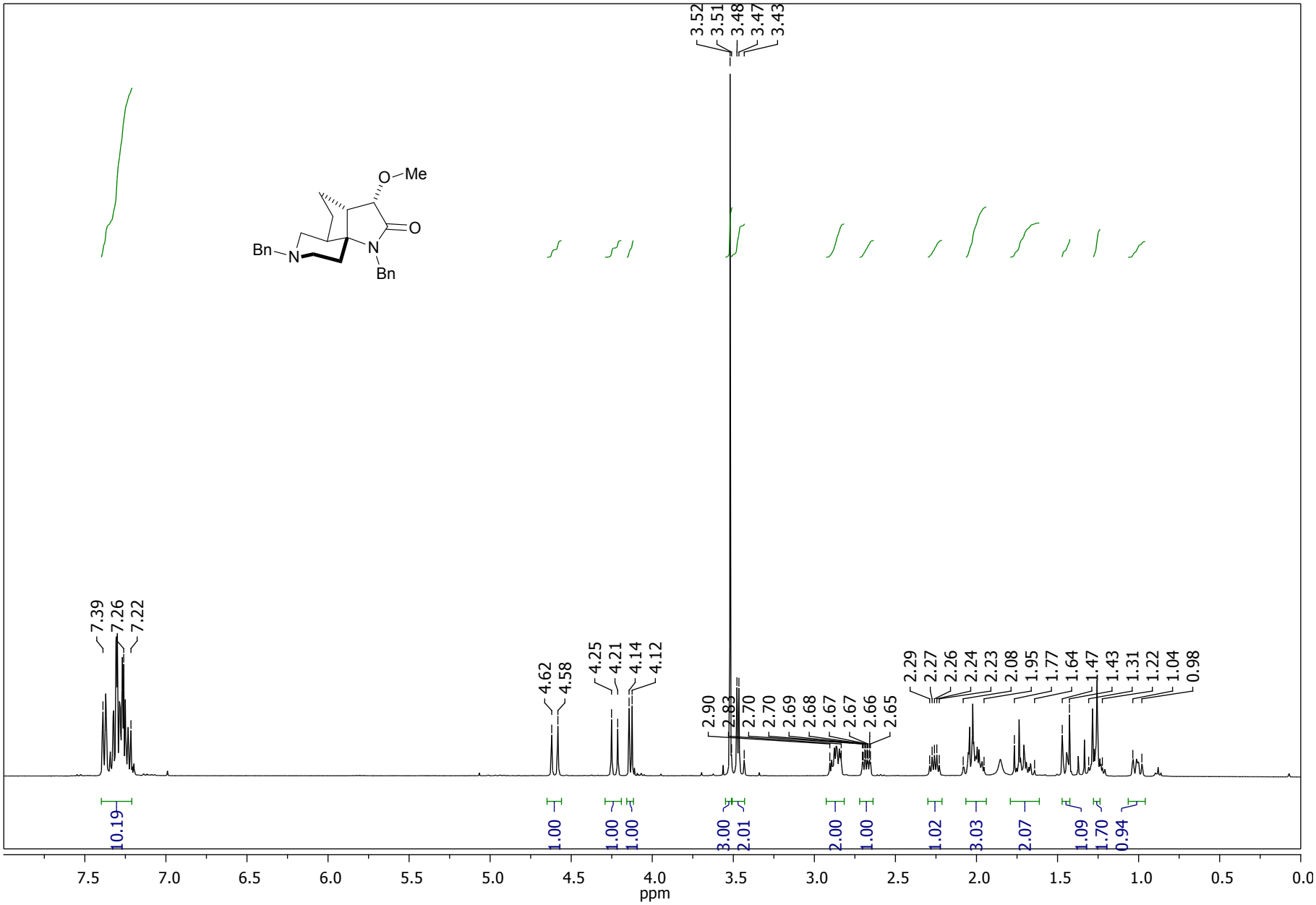
^{1}H NMR (400 MHz, $CDCl_3$) **(11b)**



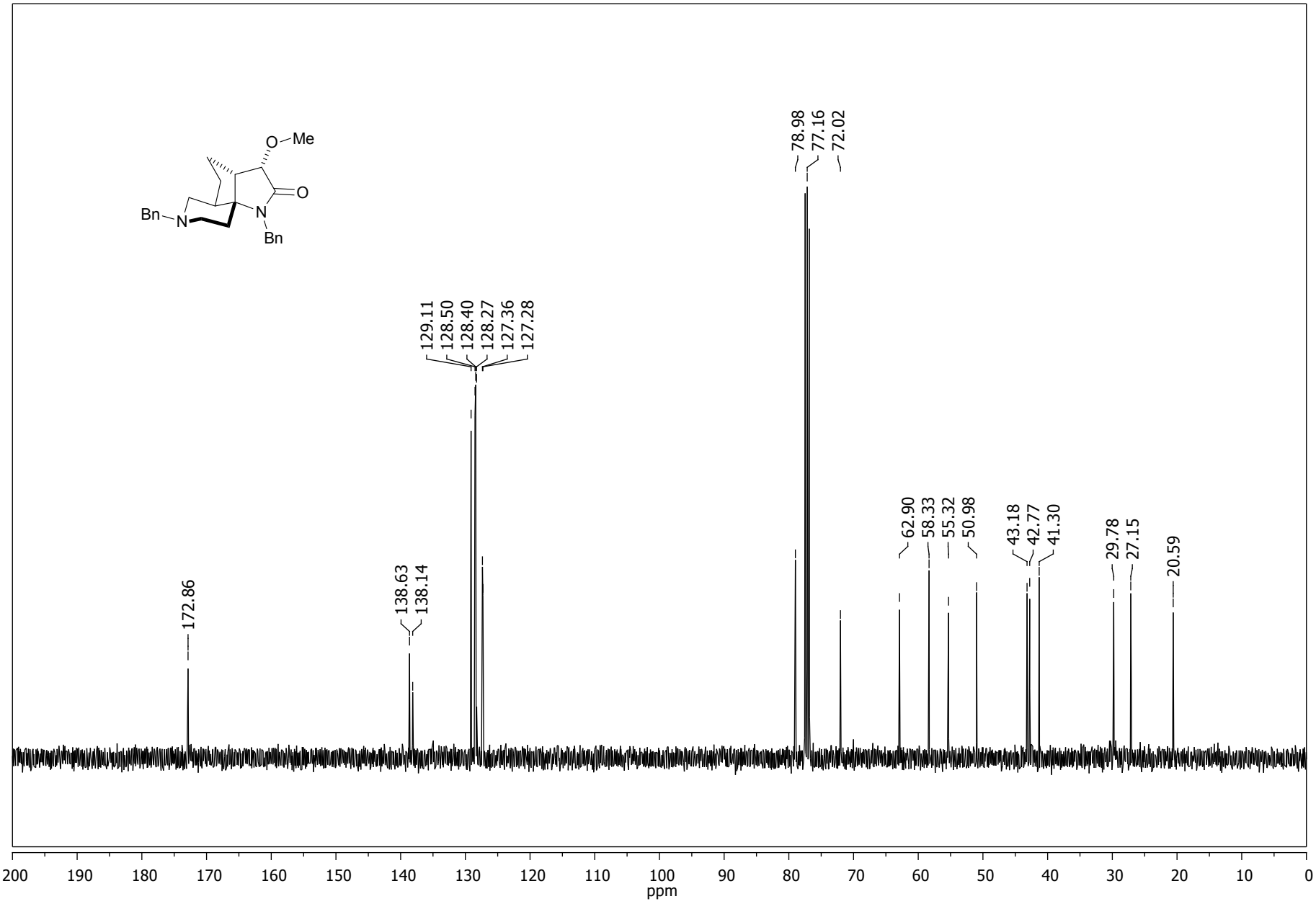
^{13}C NMR (100 MHz, $CDCl_3$) **(11b)**



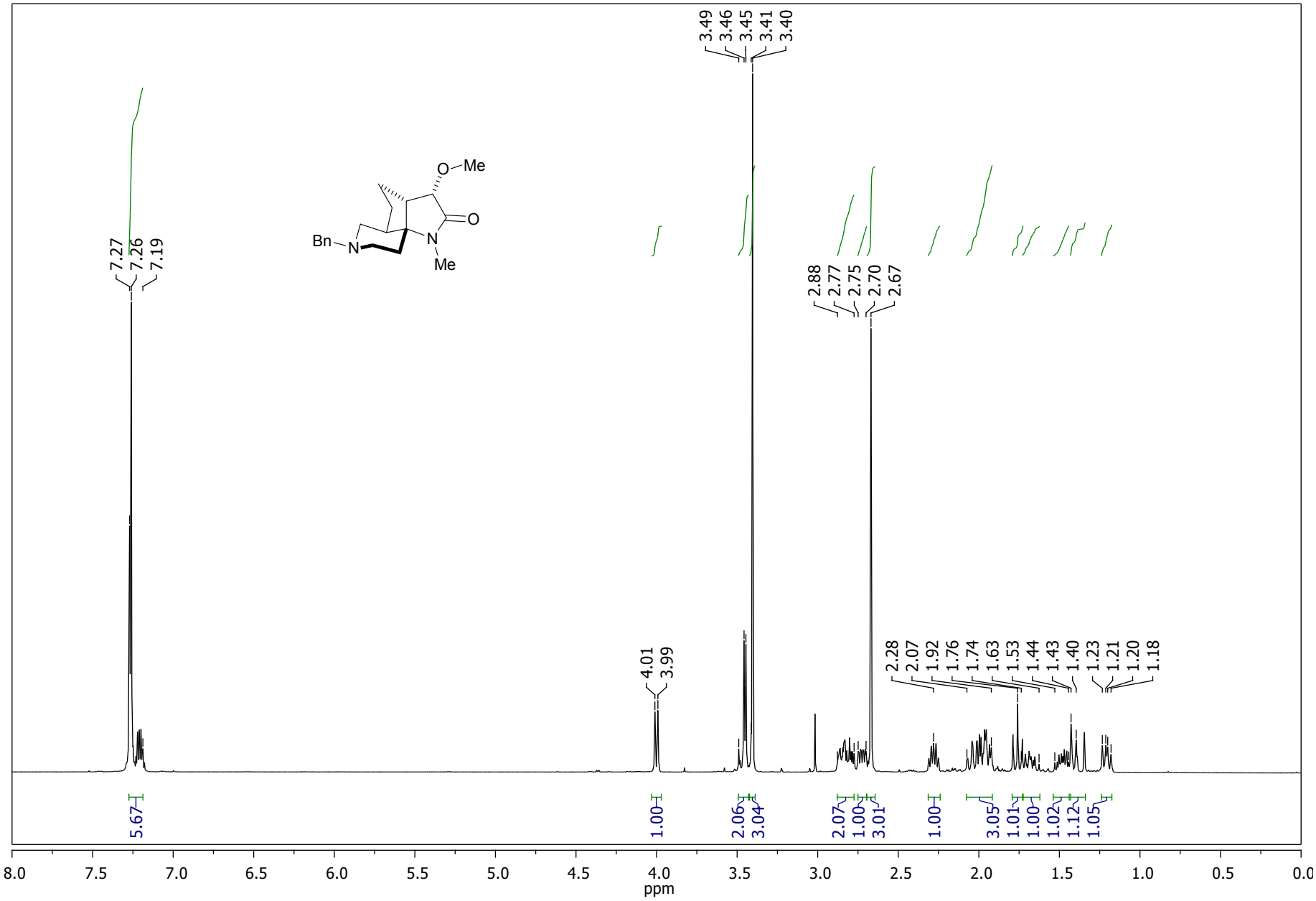
^{1}H NMR (400 MHz, $CDCl_3$) **(12a)**



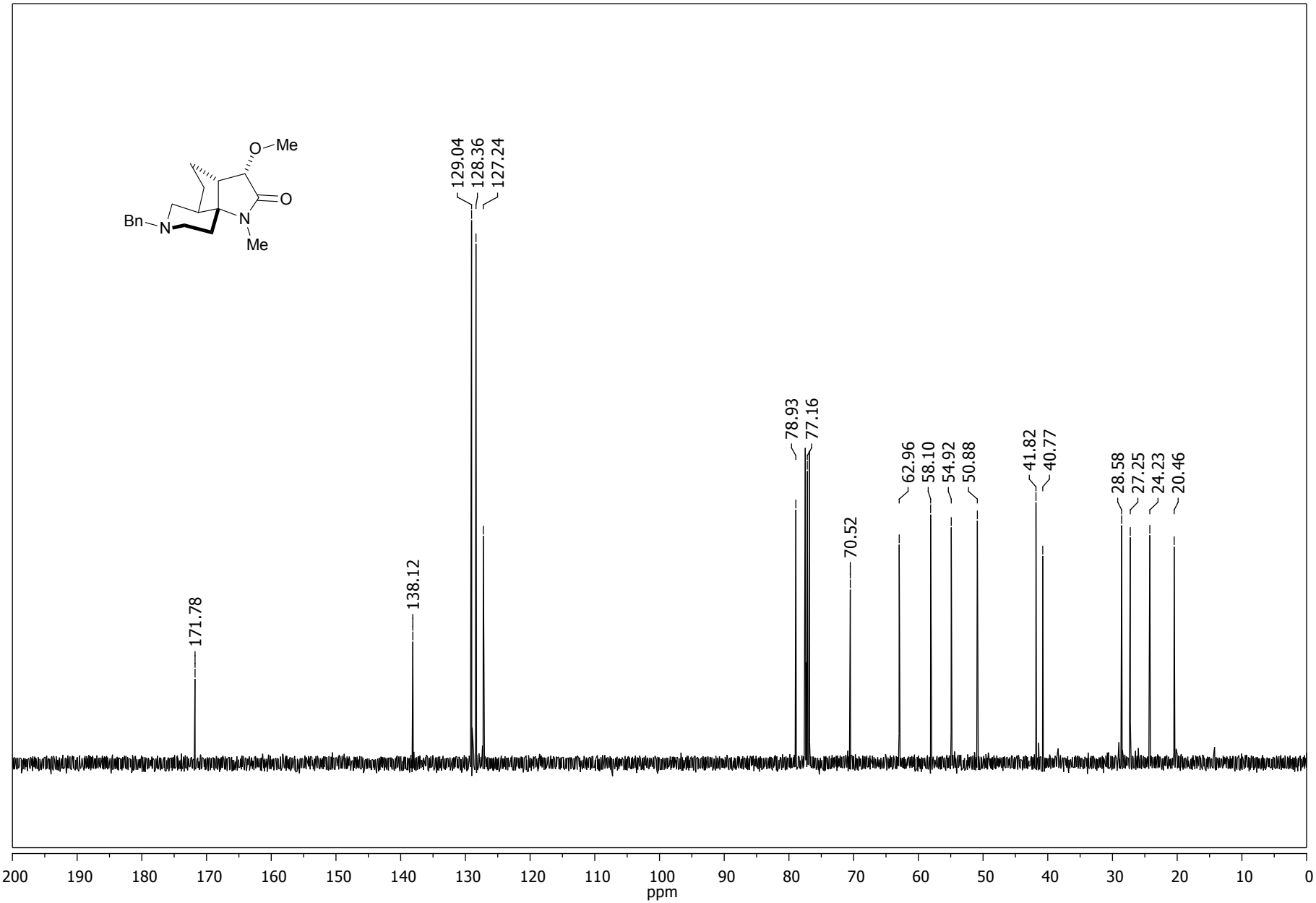
^{13}C NMR (100 MHz, $CDCl_3$) **(12a)**



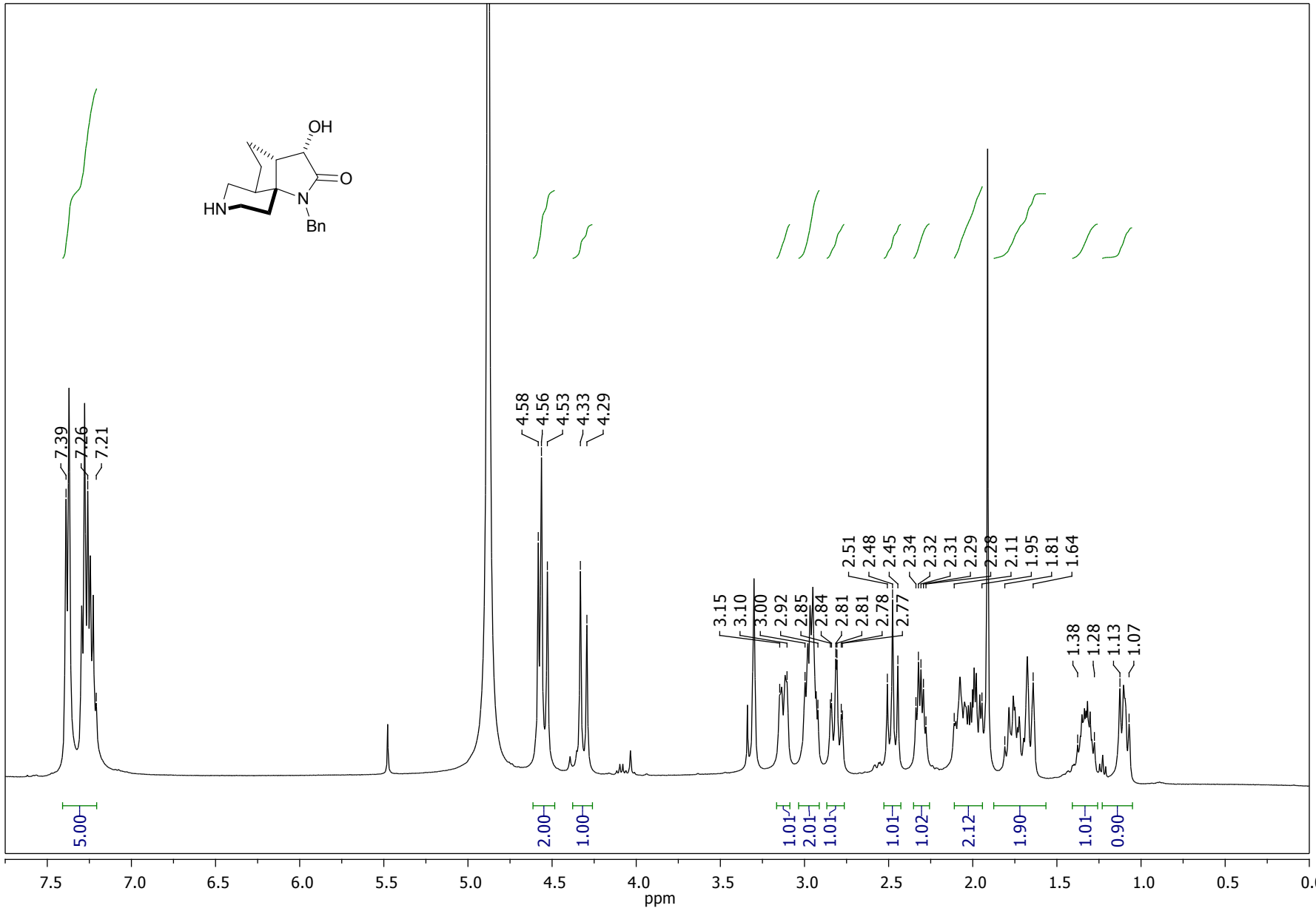
^{1}H NMR (400 MHz, $CDCl_3$) **(12b)**



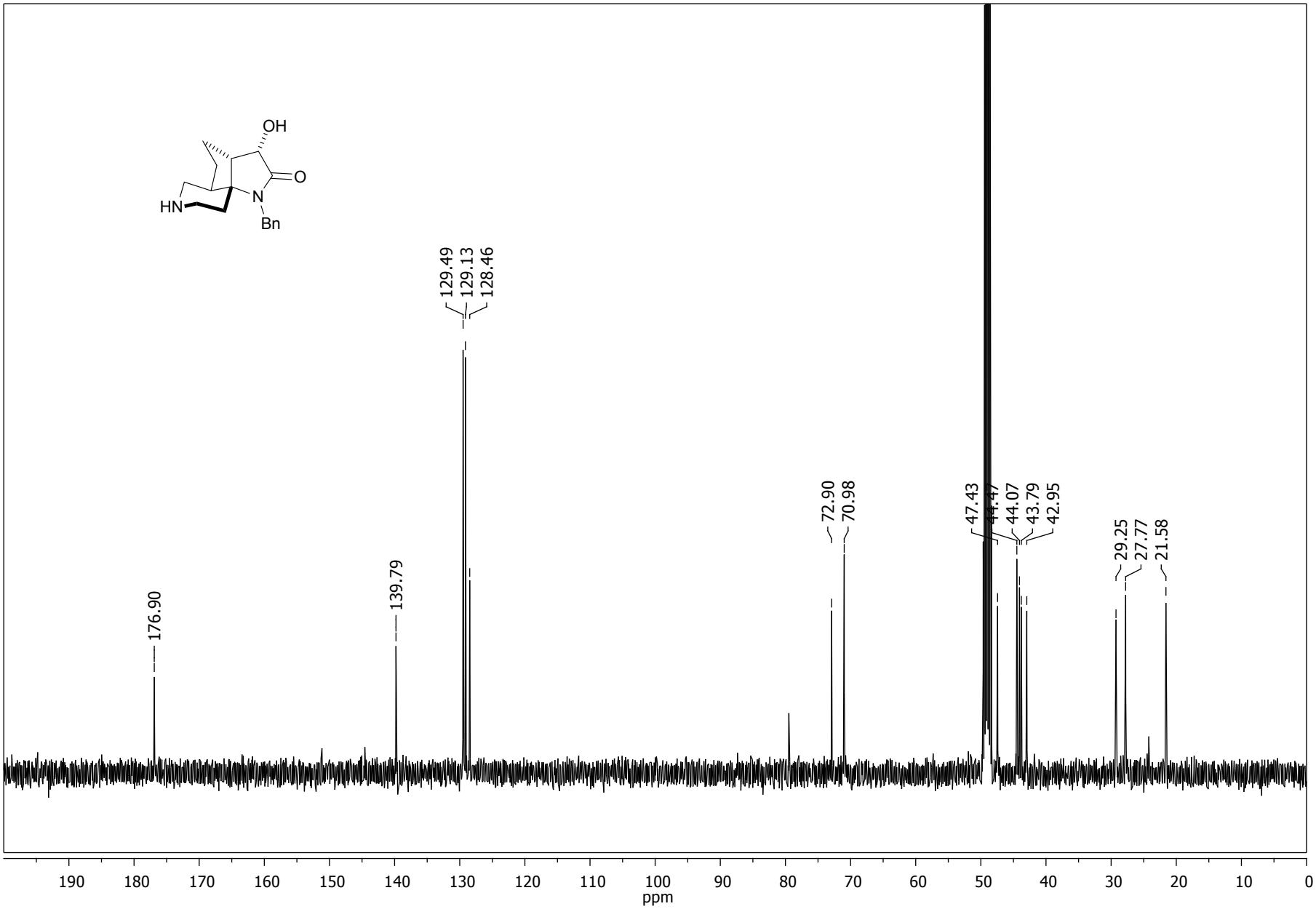
^{13}C NMR (100 MHz, $CDCl_3$) **(12b)**



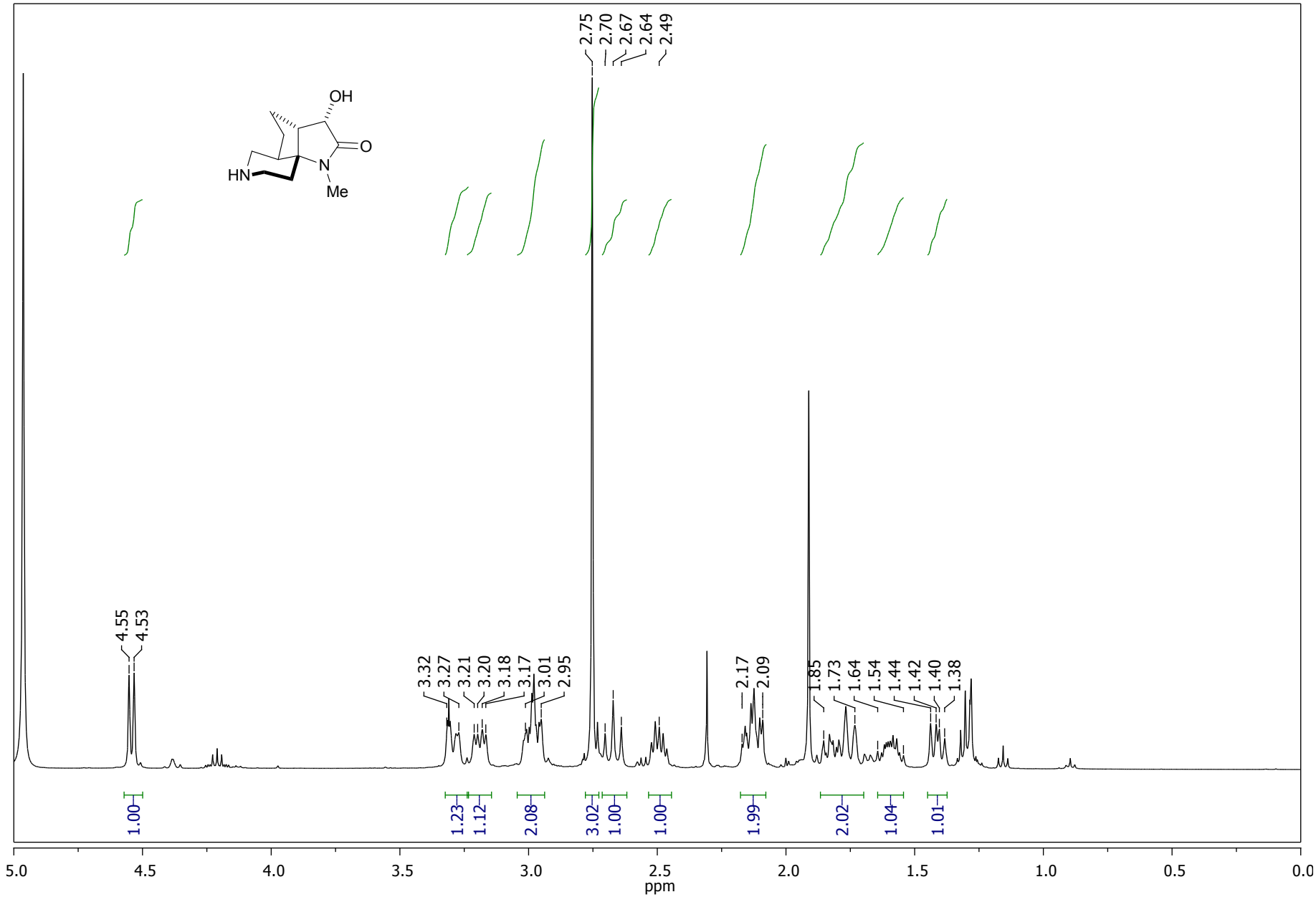
^{1}H NMR (400 MHz, CD_3OD) **(13a)**



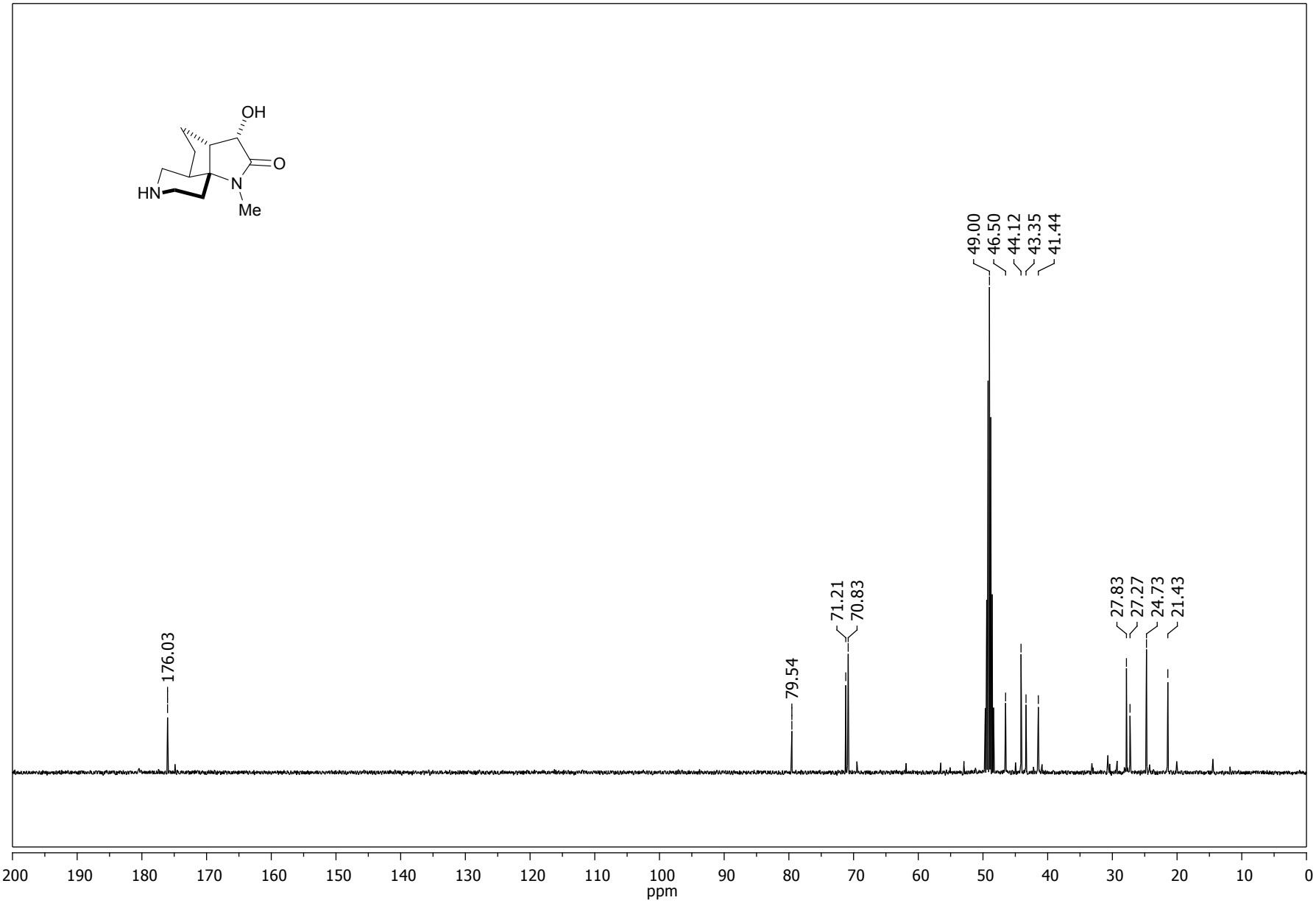
^{13}C NMR (100 MHz, CD_3OD) **(13a)**



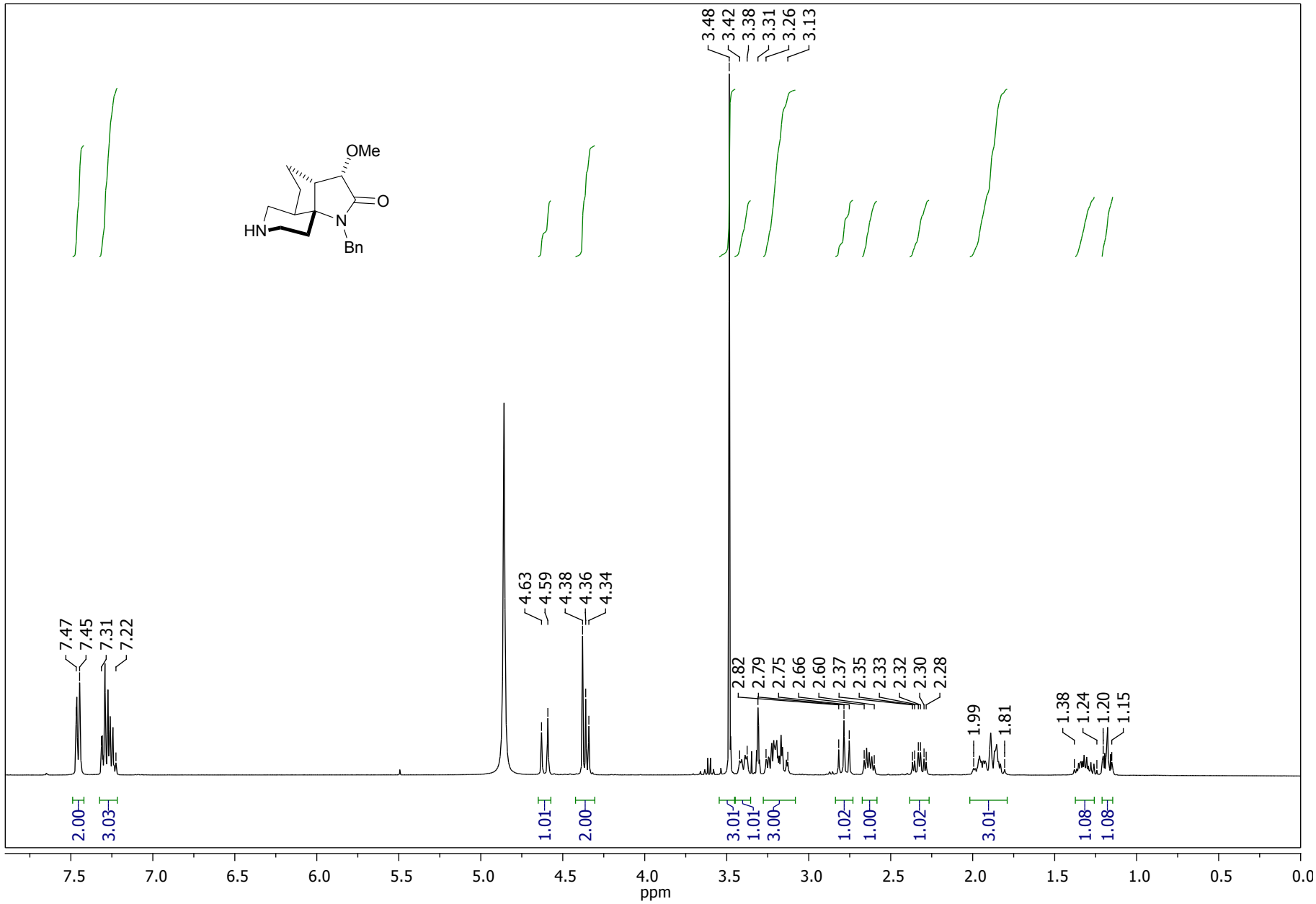
^{1}H NMR (400 MHz, CD_3OD) **(13b)**



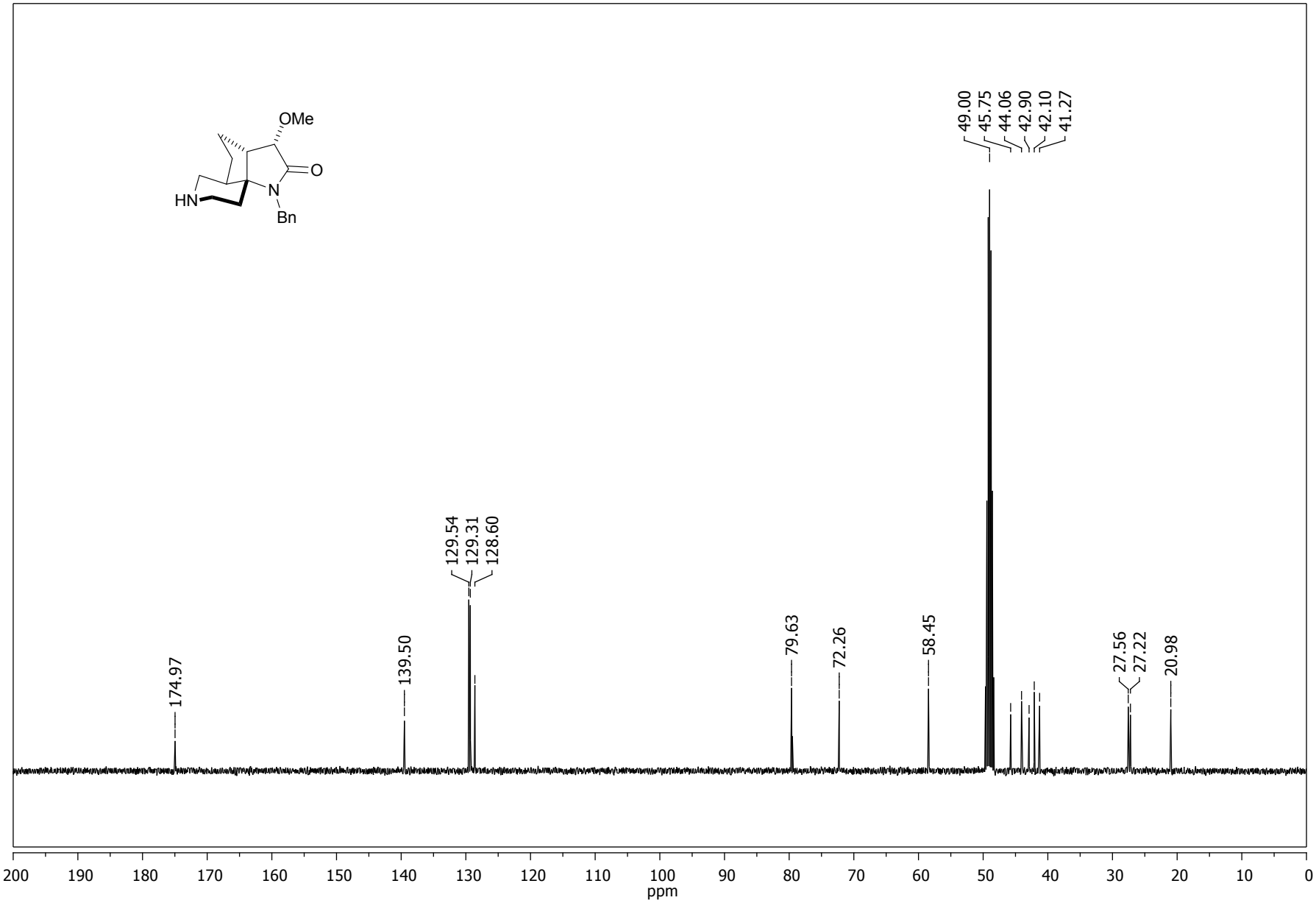
^{13}C NMR (100 MHz, CD_3OD) **(13b)**



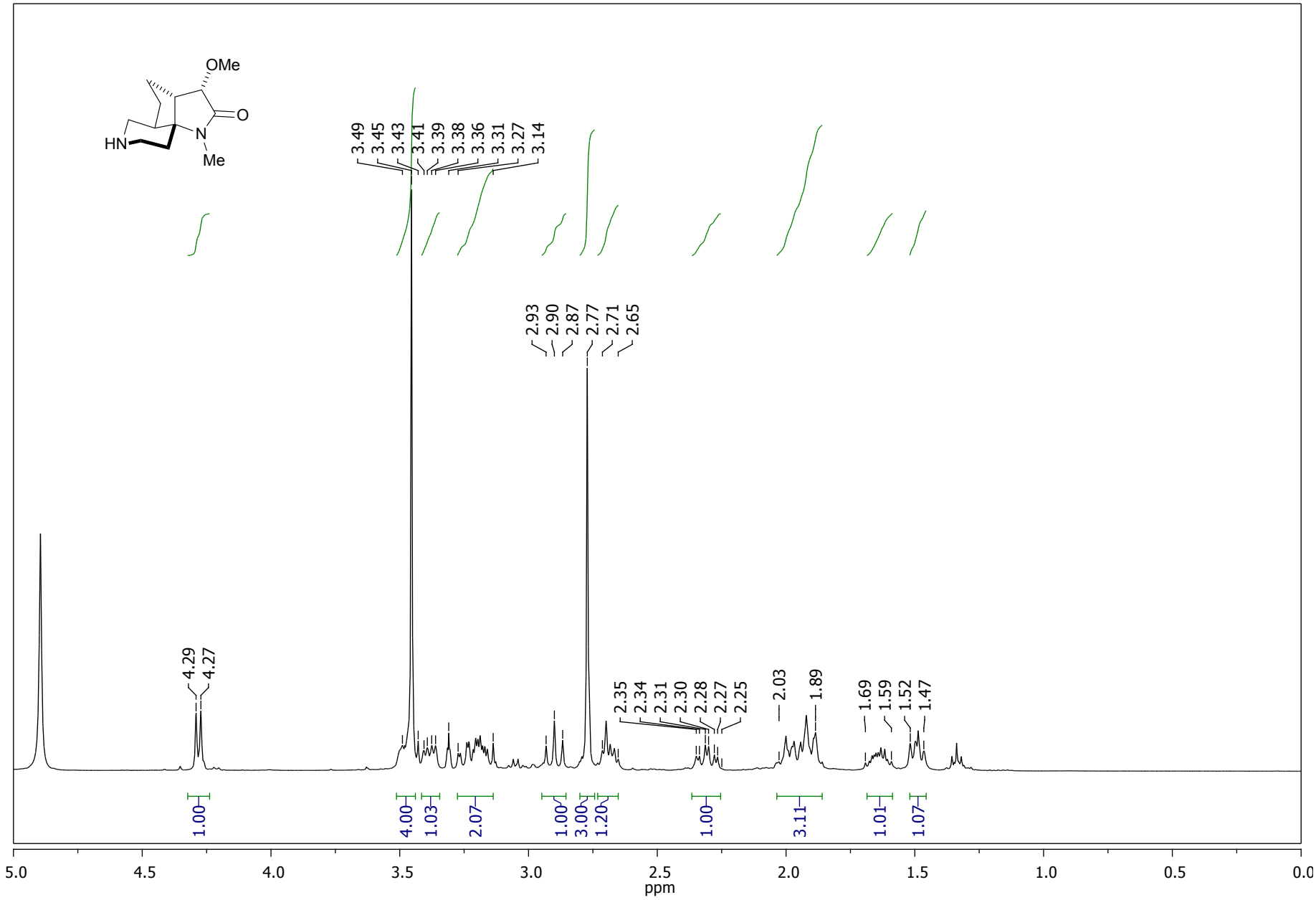
^{1}H NMR (400 MHz, CD_3OD) **(13c)**



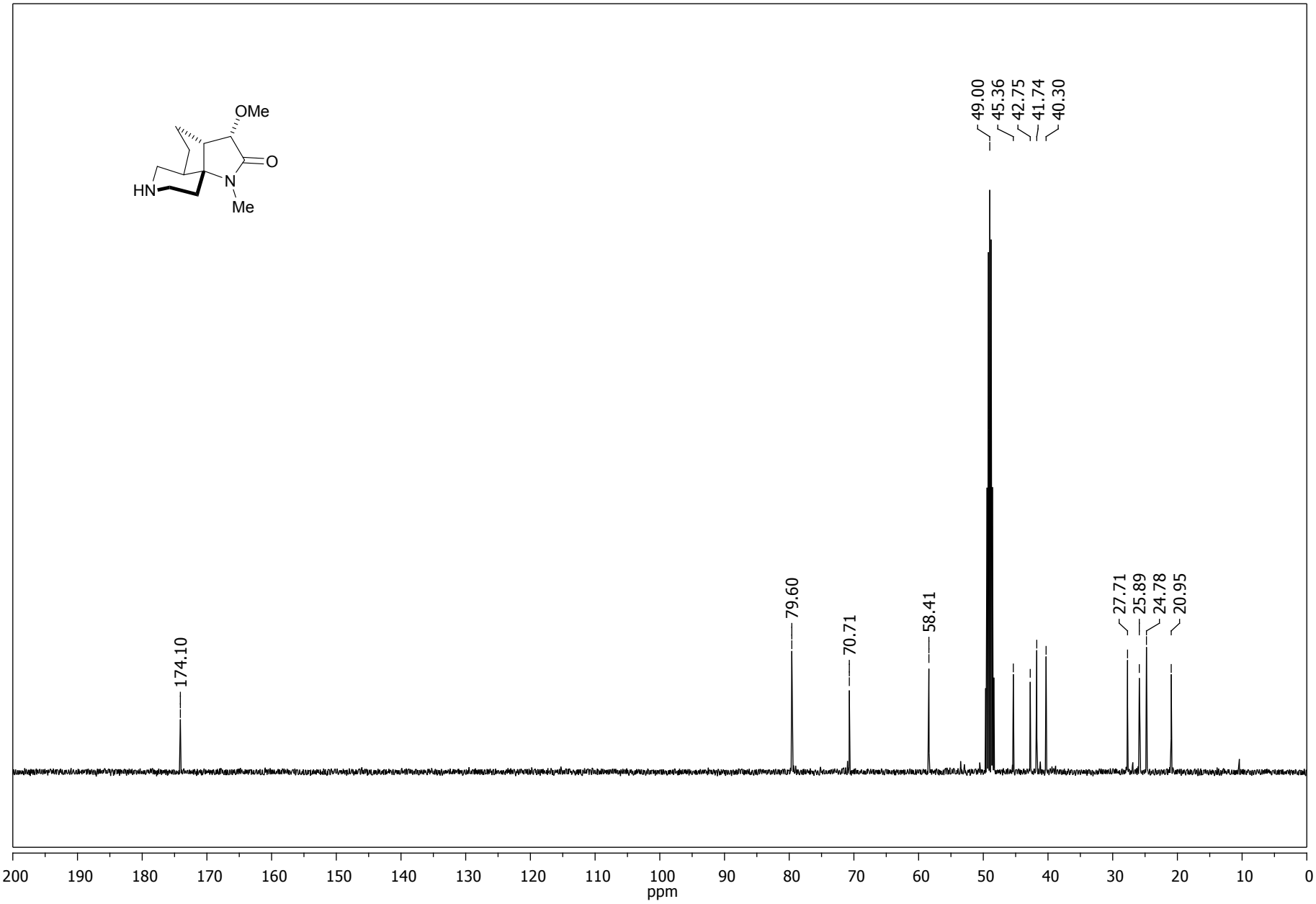
^{13}C NMR (100 MHz, CD_3OD) **(13c)**



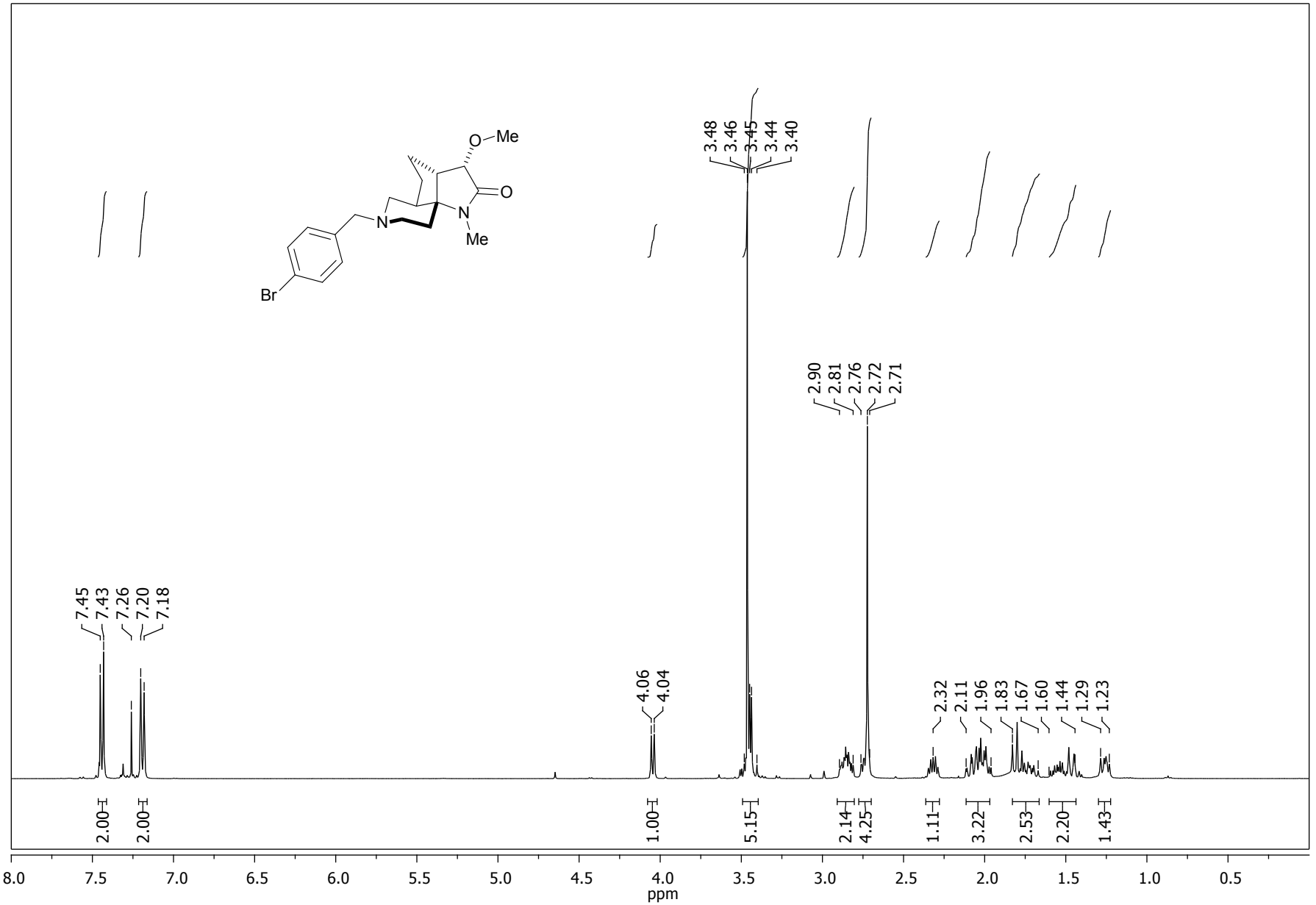
^{1}H NMR (400 MHz, CD_3OD) **(13d)**



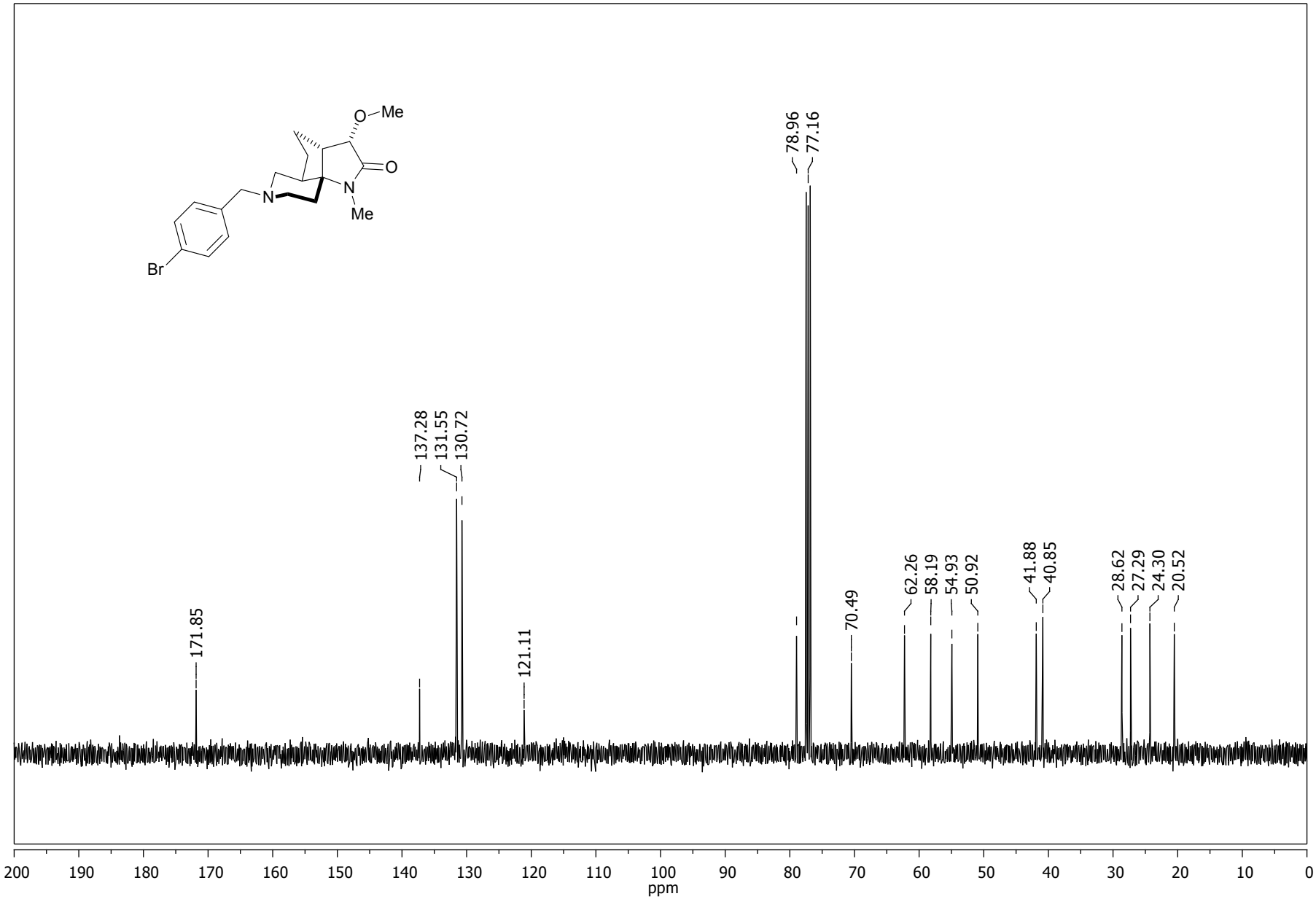
^{13}C NMR (100 MHz, CD_3OD) **(13d)**



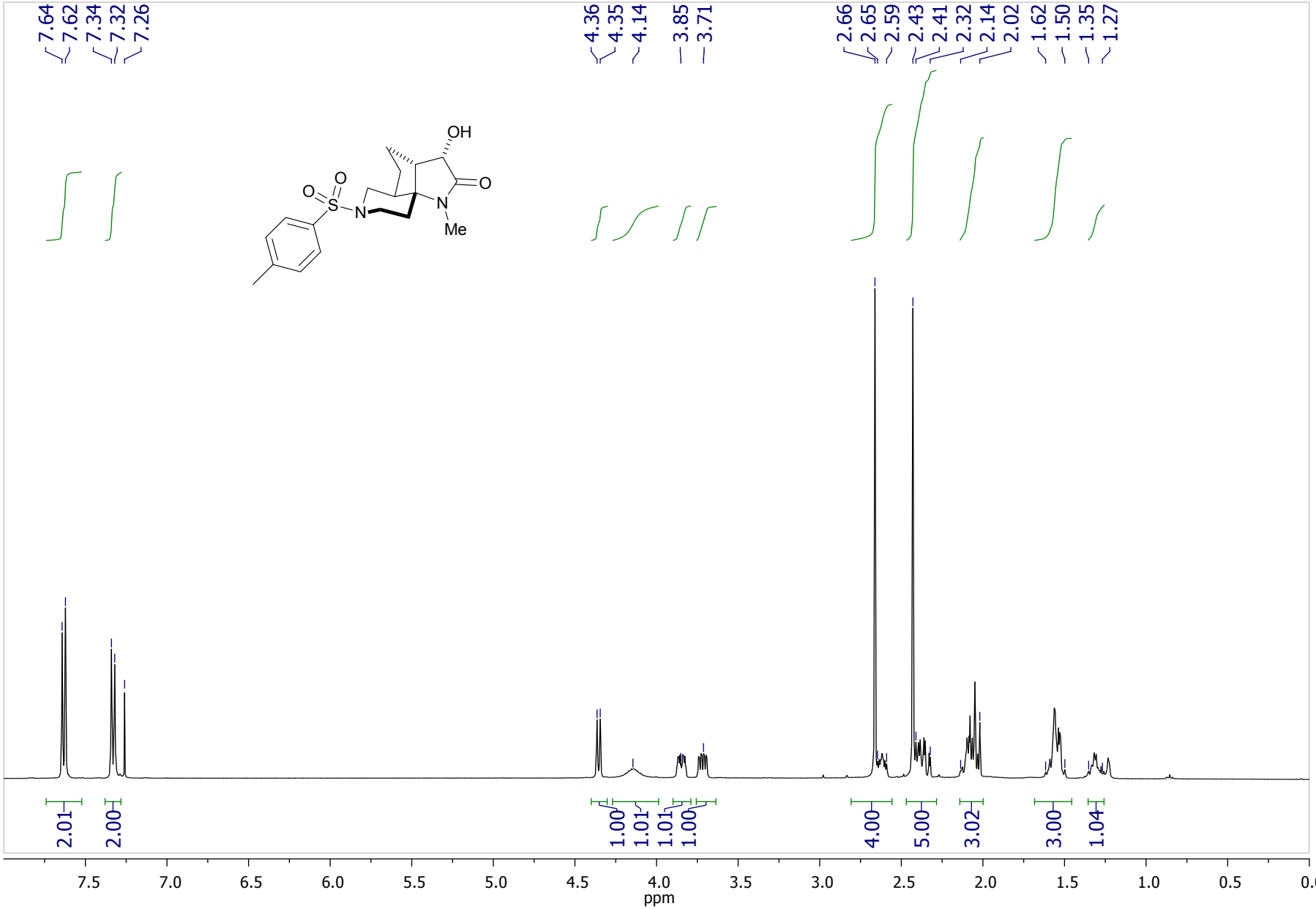
^{1}H NMR (400 MHz, $CDCl_3$) **(1c)**



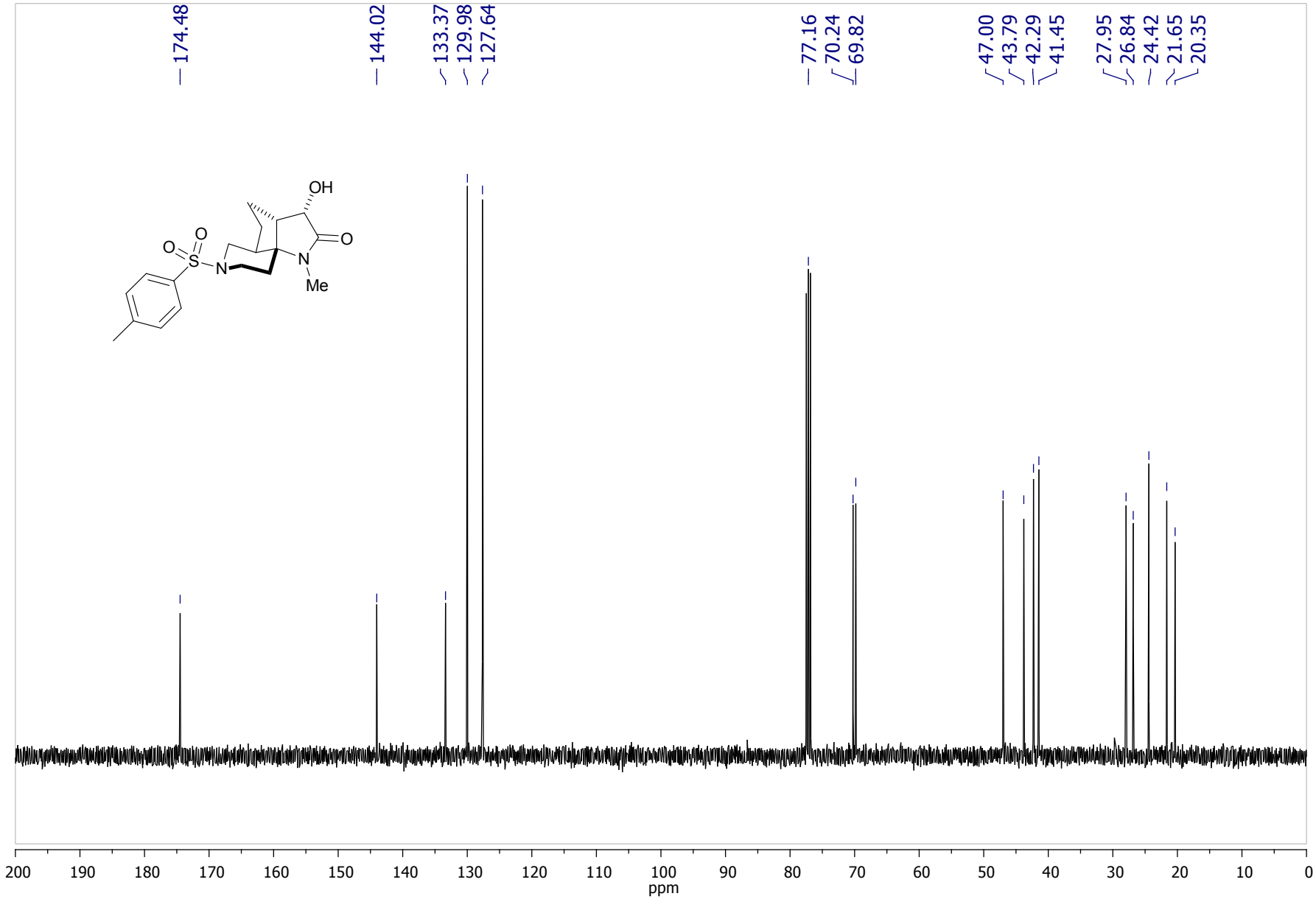
^{13}C NMR (100 MHz, $CDCl_3$) **(1c)**



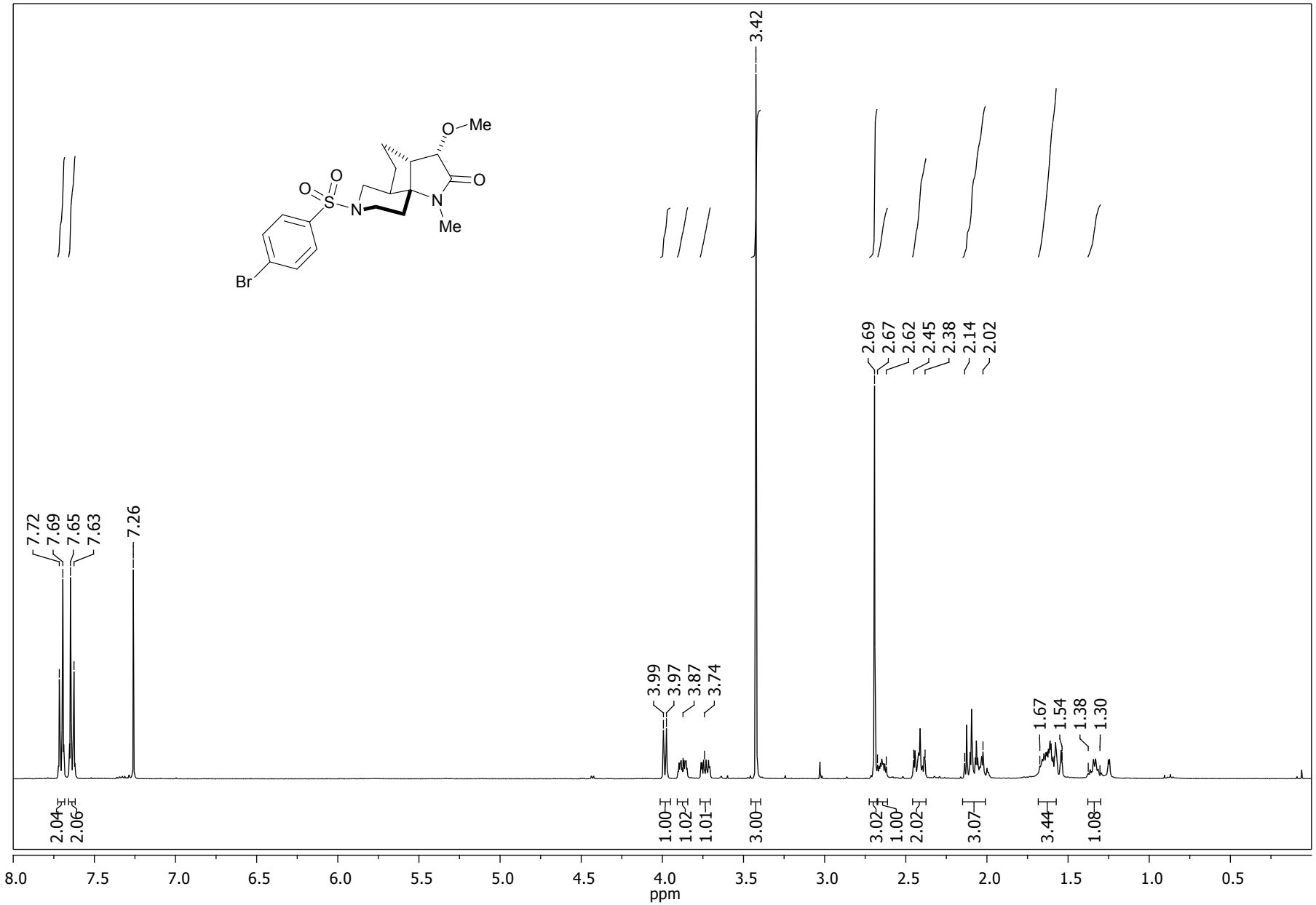
^{1}H NMR (400 MHz, $CDCl_3$) **(1a)**



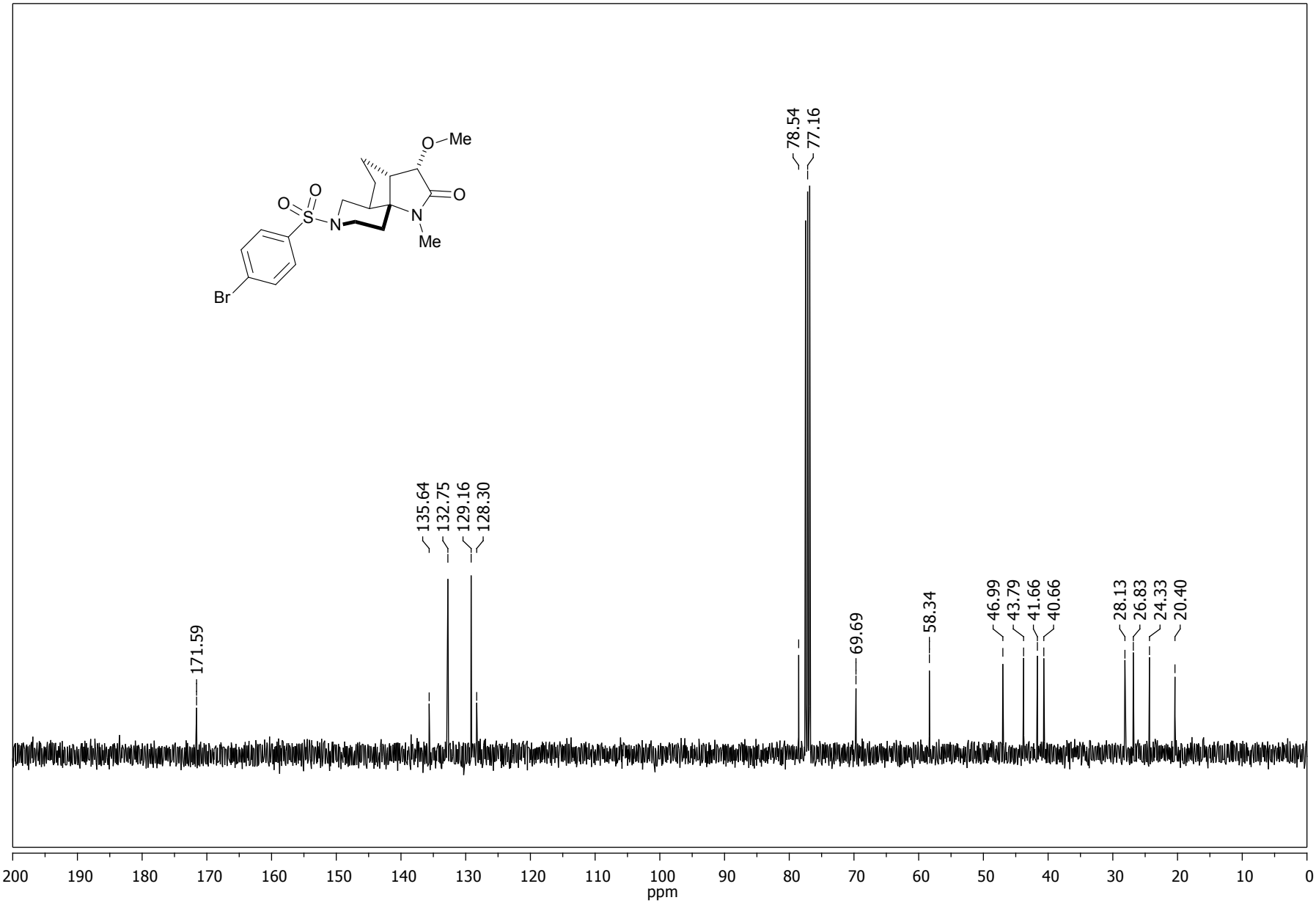
^{13}C NMR (100 MHz, $CDCl_3$) **(1a)**



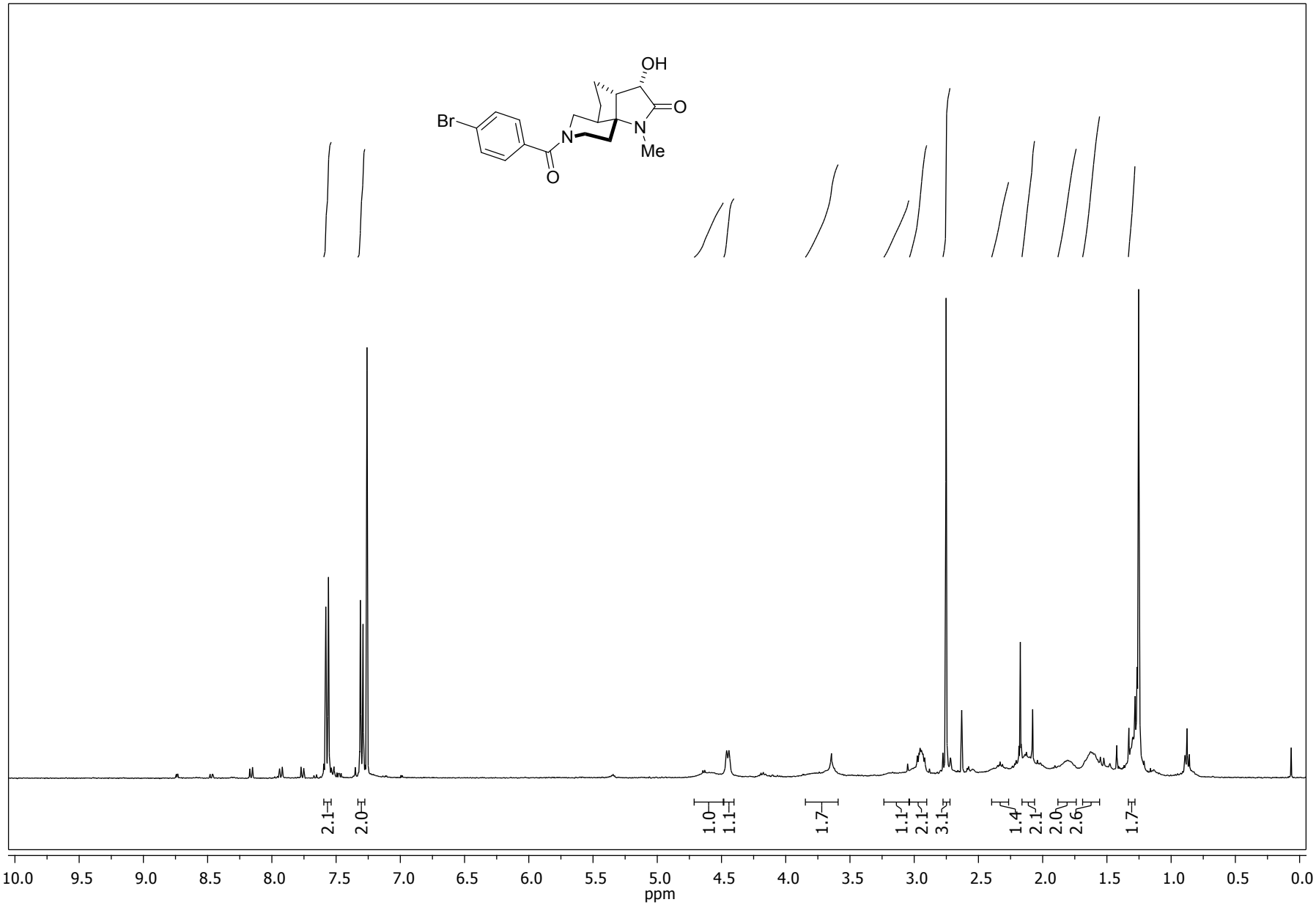
^{1}H NMR (400 MHz, $CDCl_3$) **(1d)**



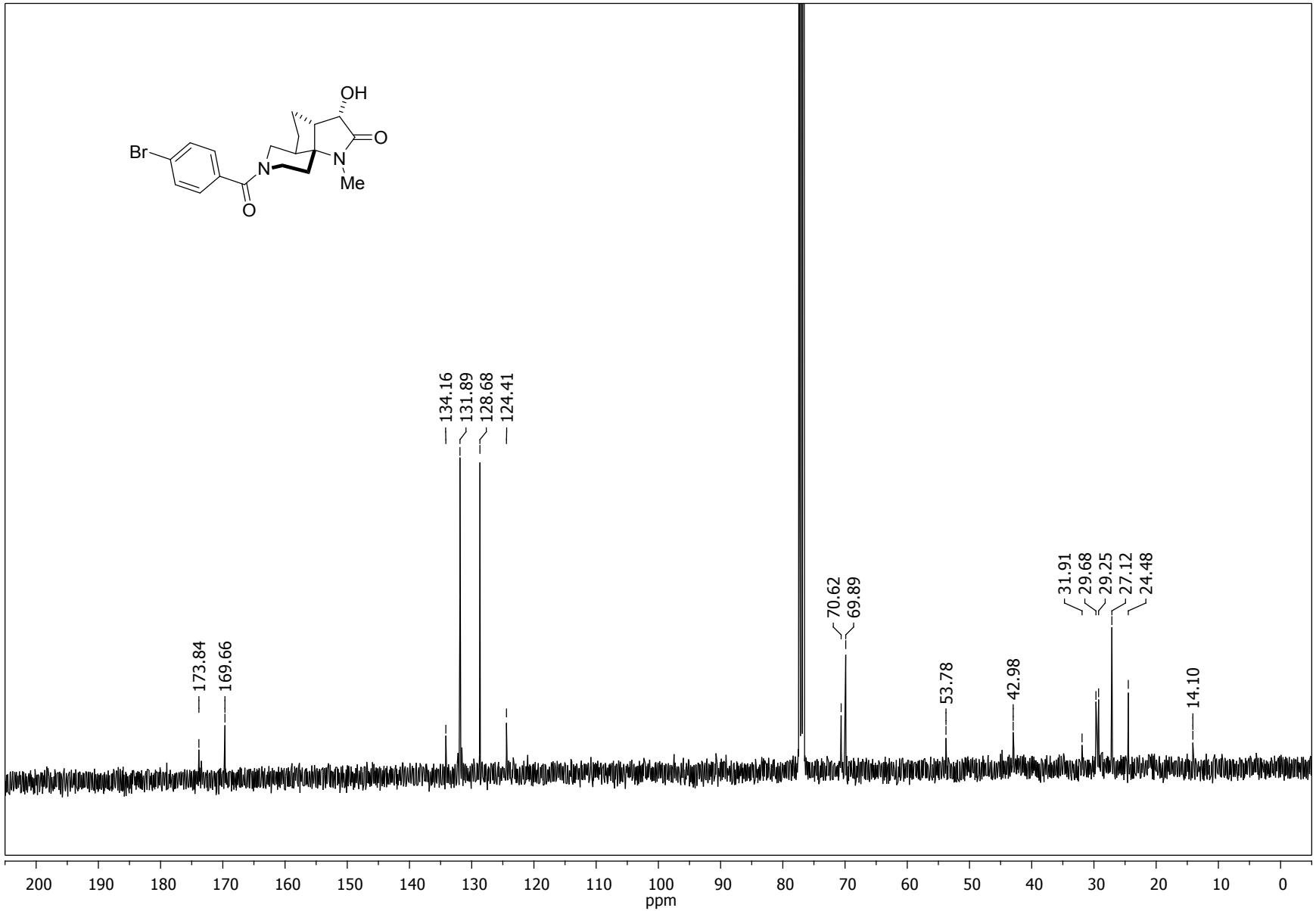
^{13}C NMR (100 MHz, $CDCl_3$) **(1d)**



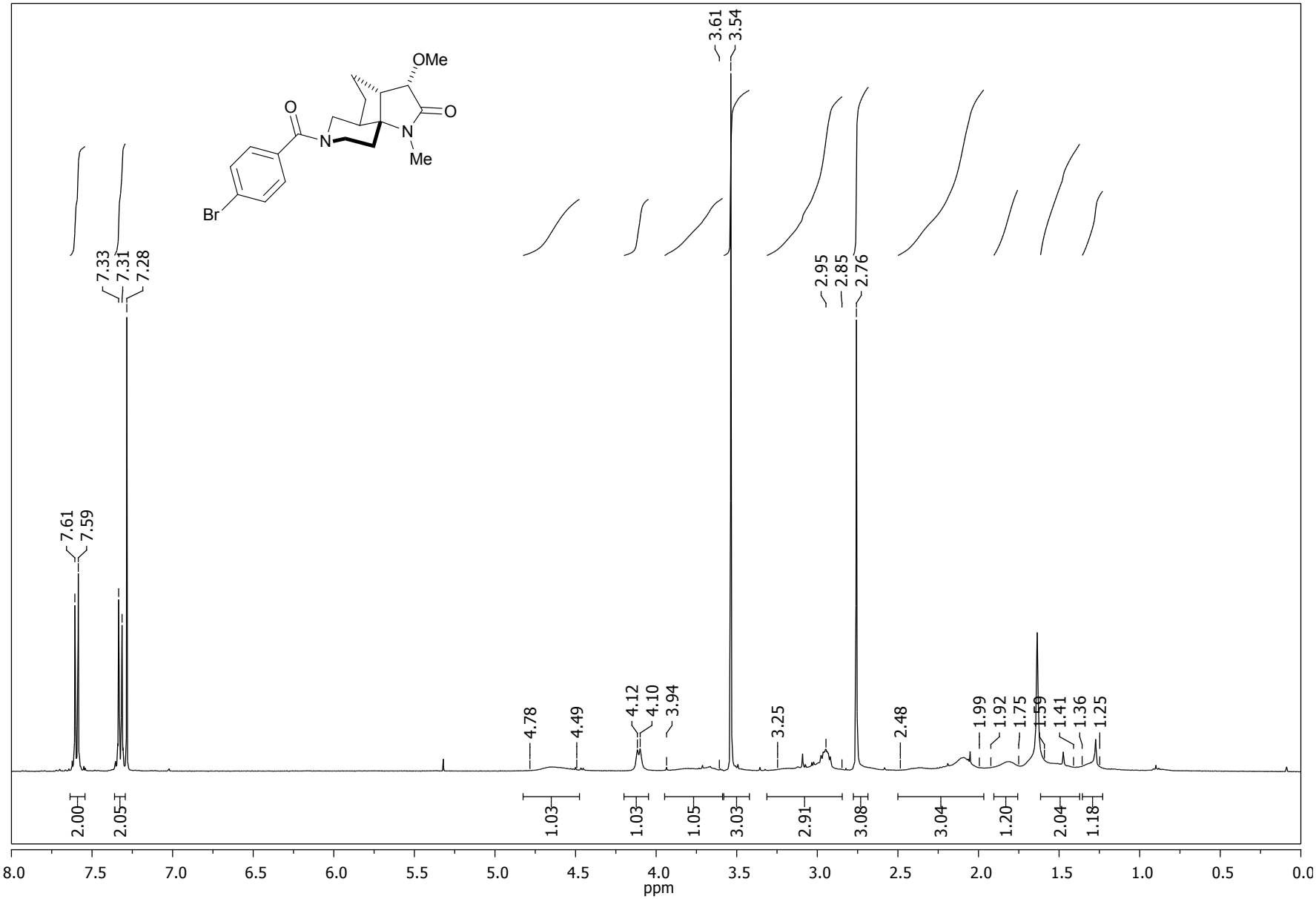
^{1}H NMR (400 MHz, $CDCl_3$) **(1b)**



^{13}C NMR (100 MHz, $CDCl_3$) **(1b)**



^{1}H NMR (400 MHz, $CDCl_3$) **(1e)**



^{13}C NMR (100 MHz, $CDCl_3$) **(1e)** (*Note: unable to see all carbon signals*)